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EXPERIMENTAL UROLITHIASIS III. PREVENTION AND DISSOLUTION OF CALCULI BY ALTERATION OF URINARY pH

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In previous publications a method was presented for the experimental production of urinary calculi by the introduction of a foreign body into the bladder of rats.[1] It was also demonstrated that foreign body calculi could be prevented by producing chronic diuresis.[2] In the animals where the stones failed to dissolve a markedly alkaline urine was found. Culture revealed that the urine of these animals contained a urea-splitting organism of the Pasteurella group.

A few experiments were done therefore to demonstrate the effect of infection with this organism on stone growth When a foreign body infected with the Pasteurella organism was implanted into the bladders of rats, the urine became intensely alkaline and marked calculus formation occurred. Most of these animals died from systemic infection before the end of the test period. Two rats which survived four weeks produced 324 mg. and 108 mg. of stone. In a few animals a suspension of the organisms was injected directly into the bladder without the introduction of a foreign body. About half of these animals developed urinary infection, alkalinuria, and calculi. These calculi, as well as all others discussed in this paper, appear to be composed chiefly of magnesium ammonium phosphate hexahydrate ($MgNH_4PO_4 \cdot 6H_2O$).

It is apparent that either the infection per se, or the alkalinity produced by the urea-splitting infection markedly influenced calculus formation in the above experiments. To test the effect of urinary pH alone in the absence of infection, stone formation upon sterile foreign bodies was studied in animals whose diets were altered by the addition of sodium bicarbonate or ammonium chloride.

METHODS

Adult male rats weighing approximately 200 to 250 gm. were used throughout these experiments. Calculi were produced in the same manner as that previously reported by introducing small pieces of zinc into the bladder to serve as the stimulus to stone formation. Where stone weights are given in this paper, the weight of the zinc foreign body nucleus has already been subtracted. The control diet was the same as that used in all previously reported experiments, i.e., powdered Purina fox chow checkers. To acidify the urine, ammonium chloride (1.5 per cent by weight) was added to the control diet. A similar amount of sodium bicarbonate was used in a third diet to produce an alkaline urine. The diets were well tolerated as judged by food consumption and weight gain.

This investigation was supported in part by a research grant from the National Institutes of Health, Public Health Service.

[1] Vermeulen, C. W., et al.: Experimental urolithiasis I. Development of calculi upon foreign bodies surgically introduced into bladders of rats. J. Urol., 64: 541, 1950.

[2] Grove, W. J., et al: Experimental urolithiasis II. The influence of urine volume upon calculi experimentally produced upon foreign bodies. J. Urol., 64: 549, 1950.

Our experiments were of two types. One tested the effect of pH on stone prevention while the other tested the effect of acidification on stones already present. In the first experiment (preventive) the rats were divided into three groups. Immediately after the initial implantation of the foreign body one group of rats was given the control diet, another group was placed on the acid diet, while the third group received an alkaline diet. At the end of 6 weeks the animals were sacrificed and the stones removed and weighed. In the second experiment (curative) stones were first produced on foreign bodies by the standard method with the control diet. At the end of 2 months the stones were removed, weighed and immediately re-implanted. At this time the animals were divided into two groups after discarding those in which no stone had formed. One group remained on the control diet; the other group was shifted to the acidifying diet containing ammonium chloride.

At regular intervals during the experiment the rats were placed in special metabolism cages. The urine was quantitatively collected for 48 hours and the magnesium and phosphorus excretion determined. It is realized that quantitative collection of such small volumes is open to large error and that the results obtained can only be considered as approximations. Urine for culture and pH determination was obtained by aspiration of the bladder at the time of operation. Cultures were made on blood agar and Brewer's anerobic medium. The pH was also obtained from time to time during the experiments on freshly voided urine collected by pipette.

TABLE 1. *Summary of urine findings*

	AVERAGE pH	QUANTITATIVE URINE CHEMISTRY			
		Number of Rat Days	Aver Vol. cc/day	Magnesium mg %	Phosphorus mg. %
Control rats	6.41	54	14.6	37.1	142
Acidified rats (1.5% NH_4Cl)	5.74	52	13.6	49.6	235
Alkalinized rats (1.5% $NaHCO_3$)	7.25	35	16.8	49.8	135

RESULTS

The urinary changes found in the different groups are summarized in table 1. It can be seen that no striking difference in urine volume occurred, but that the phosphorus excretion was markedly elevated in the group given ammonium chloride. The magnesium excretion was relatively less affected. Urine produced by the rats given sodium bicarbonate differed but little from the controls in magnesium and phosphorus content.

Of the total of 56 rats in the first (preventive) experiment, urine for culture was obtained from 48. All but 4 were sterile. Obviously infection can be eliminated as an important factor in this experiment. In the second experiment (curative) a somewhat higher incidence of positive urine culture occurred, but no correlation could be made between stone growth and infection.

The amounts of stone produced in the different groups in the first experiment (preventive) are seen in figure 1 and table 2. Negligible stone formation occurred in the acidified group of 21 animals. On the other hand the 17 animals in the control group produced an average calculus of 60 mg. Statistical analysis showed that the probability (p) of this difference occurring by chance alone is much less than one in one hundred (.01). The alkalinized rats produced slightly more stone than the controls, but the difference was not statistically significant.

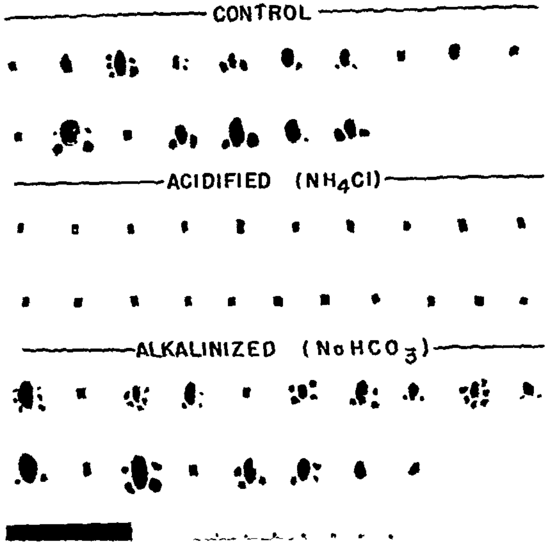

FIG. 1. (Experiment 1, preventive). Bladder contents of control, acidified, and alkalinized rats 6 weeks after implantation of foreign bodies in bladders. Small square naked foreign bodies are seen where stones failed to form. Where stone formation occurred, foreign bodies are buried in large stones. Daughter calculi, when found, have been grouped about their respective foreign body stones.

TABLE 2. *Experiment 1 (preventive). Effect of pH on growth of calculus in six weeks*

	NUMBER OF RATS OBSERVED	AVERAGE WT. OF CALCULUS IN MG.
Control rats	17	60.4 ± 20.9*
Acidified rats (1.5% NH_4Cl)	21	1.6 ± 1.1
Alkalinized rats (1.5% $NaHCO_3$)	18	70.3 ± 20.5

Statistical comparison:

Stone weight control vs. acidified—$t = 3.13$

* Standard Error

The results from 39 rats are available in the second experiment (curative). They are shown in figure 2 and table 3. It will be remembered that these rats had first been fed the control diet for a period of 2 months in order to form stones. Then the weight of each stone was determined at operation and the animals were divided into two groups. The rats were arranged so that both groups had approximately the same average stone weight (115 mg.). One group continued on the control diet. The other was changed to the diet containing ammonium chloride. Four weeks later, when the animals were sacrificed, it was found that the stones of the control group had continued to grow, with an average weight increase of 79 mg. On the other hand, the group given the acidifying diet showed a loss of stone weight averaging 64 mg. Fourteen of the 20 animals in the latter group showed complete dissolution of stone so that the zinc foreign body was found free in the bladder. Statistical evaluation, as expected, showed that there was a highly significant difference between the two groups (p less than .01).

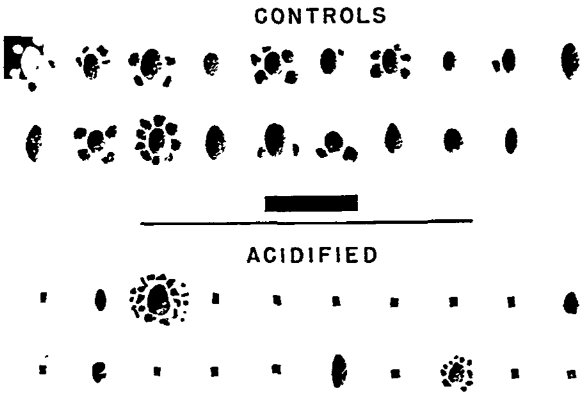

FIG. 2. (Experiment 2, curative). Four weeks previous to this photograph the average weight of the stones in each group was the same (115 mg.). Now, average weight of control group is 195 mg. Other group was changed to acidifying diet and stones dissolved leaving an average stone weight of 51 mg. for this group. Of 20 stones in acidified group, 14 dissolved completely, leaving zinc free.

TABLE 3. *Experiment 2 (curative). Dissolution of calculus by acidification for four weeks*

	CONTROL DIET	ACIDIFIED DIET
Number of rats observed	19	20
Average initial stone weight	116 6 mg	115 1 mg
Average final stone weight	195 3 mg.	51.4 mg.
Average stone weight change during 4 weeks on stated diet	+78 7 mg.	−63 7 mg

Statistical *comparison:*
Stone weight change control vs. acidified—t = 4 254

DISCUSSION

The calculi produced in our rats are apparently composed chiefly of magnesium ammonium phosphate hexahydrate ($MgNH_4PO_4 \cdot 6H_2O$), as reported in the first paper of this series. It is curious that stones composed of this material developed in a urine that was slightly acid in reaction, as shown in the rats given the control diet. This type of stone has been thought to occur only in an alkaline urine and characteristically appears where the urinary system is infected with urea-splitting organisms leading to an intensely alkaline urine. Previous work has indicated that stones containing magnesium are not formed in an acid urine in rats.[3] In vitro studies of the solubility of magnesium ammonium phosphate in water indicate that this material is quite soluble if the pH is below 6. The sharp drop in solubility occurs over the range of pH 6 to pH 7.5. It is therefore not surprising that stones can form at a pH of 6.4, as in our control rats, and that acidification prevents them.

On the other hand, it was not expected that acidification would result in early dissolution of a pre-formed stone. There is remarkably little evidence in the clinical literature to indicate that calculi can be dissolved in vivo by methods other than irrigation with solvents. Higgins[4] has presented clinical evidence in this connection. From the experimental side, both Higgins and Hammarsten[5] have reported dissolution of rat calculi by change of diet. We believe that the quantitative method used by us offers a far clearer means of demonstrating calculus dissolution. We are likewise of the opinion that these experiments show clearly that the process of stone formation is a reversible one.

SUMMARY

The influence of urinary pH on experimental calculi was tested in rats. Two types of experiments were used. The stimulus to stone formation was a foreign body surgically implanted into the bladder. Ammonium chloride added to the diet was used to lower the urinary pH. In one experiment the addition of ammonium chloride prevented the formation of calculi in all of 21 animals. In the second experiment where acidification was begun only after stones had already formed, complete dissolution of the calculi occurred in 14 or 20 animals. Suitable control groups accompanied each experiment.

---

[3] Prien, E. L.: Studies in urolithiasis 2. Relationship between pathogenesis, structure, and composition of calculi. J. Urol., **61:** 821, 1949.

[4] Higgins, C. C.: Production and solution of urinary calculi. J.A.M.A., **104:** 1296, 1935.

[5] Hammarsten, G.: Dietetic therapy in the formation of calcium oxalate calculi in the urinary passages 2. Skand. Arch. f. Physiol., **80:** 165, 1938.

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EXPERIMENTAL UROLITHIASIS IV: PREVENTION OF MAGNESIUM AMMONIUM PHOSPHATE CALCULI BY REDUCING THE MAGNESIUM INTAKE OR BY FEEDING AN ALUMINUM GEL

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In the first paper of this series an experimental method for the study of urolithiasis was presented.[1] The method is based upon the observation that bladder stones can be formed quickly in rats if a foreign body is placed in the bladder. Chemical analysis indicated that the stones were composed primarily of magnesium ammonium phosphate hexahydrate. In other papers it was shown that marked diuresis[2] or marked acidification of the urine[3] prevented stone formation. In the experiments presented here we have continued the study of these stones by observing the relation between stone growth and the concentration of magnesium and phosphorus in the urine.

DESCRIPTION OF EXPERIMENTS

The methods used were, in general, the same as those described in previous reports. Adult male rats weighing 200–250 gm. were used. A standard foreign body consisting of a square piece of zinc was placed in the bladder of each animal to serve as the nucleus upon which stone could form. After 6 weeks the bladder of each animal was exposed suprapubically and urine was obtained by aspiration for culture and pH determination. The stone was then removed and weighed. By subtracting the initial weight of the zinc foreign body nucleus the amount of calculus actually produced was determined.

Experiment 1. Prevention of stone by diet low in magnesium. A synthetic diet was necessary for this experiment so that its magnesium content could be varied without altering the other components. The balanced synthetic diet described by Cannon et al.[4] was selected. The magnesium content of the Cannon diet is low when compared to our standard diet of Purina fox chow checkers. It was used without modification as our low magnesium diet. To be compared with it, another diet was prepared using the Cannon formula but in which the content of the magnesium salts was increased to three times the amount given by Cannon.

This investigation was supported by a research grant from the National Institutes of Health, Public Health Service.

We are indebted to Mr. John McLaren, of Wyeth, Inc. for generously supplying the basaljel used in these experiments.

[1] Vermeulen, C. W., Grove, W. J., Goetz, R., Ragins, H. D. and Correll, N. O.: Experimental urolithiasis I. Development of calculi upon foreign bodies surgically introduced into bladders of rats. J. Urol., **64:** 541, 1950.

[2] Grove, W. J., Vermeulen, C. W., Goetz, R. and Ragins, H. D.: Experimental urolithiasis II. The influence of urine volume upon calculi experimentally produced upon foreign bodies. J. Urol., **64:** 549, 1950.

[3] Vermeulen, C. W., Ragins, H. D., Grove, W. J. and Goetz, R.: Experimental urolithiasis III. Prevention and dissolution of calculi by alteration of urinary pH. J. Urol., **66:** 1, 1951.

[4] Cannon, P. R., Wissler, R. W., Woolridge, R. L., and Benditt, E. P.: The relationship of protein deficiency to surgical infection. Ann. Surg., **120:** 514, 1944.

A third diet, our standard Purina fox chow, was added to the experiment to allow comparison with our previous work. The calcium, magnesium and phosphorus content of these three diets are compared in table 1.

Each of the three diets was tested in a group of rats with foreign body implants. During the course of the experiment urine was obtained for quantitative analysis. The results of these analyses are shown in table 2. In general, the magnesium excretion was found to parallel the magnesium intake. It is interesting to note that the phosphorus excretion did not correspond to the phosphorus content of the different diets. On the synthetic diets it was twice as great as on the fox chow checkers despite the fact that fox chow contains four times as much phosphorus. Apparently much of the phosphorus in fox chow is in nonabsorbable form. After the animals had been on the 3 diets for 6 weeks, the experiment was terminated. At that time the average pH of the aspirated urine was found to be approximately the same in all three groups (table 2). Urine cultures were obtained in 61 of the 75 rats in the experiment. The urine was sterile in 52 of the 61 cultures with no apparent relation between infection and stone growth. The average size of the stones in the different groups is compared in table 3. The rats on the Cannon diet (low in magnesium) failed to produce stones. The same diet resulted in excellent stone growth when its magnesium content was increased. The average stone weight was even larger than that occurring with our standard diet of fox chow checkers.

TABLE 1. *Chemical composition of diets*

	CONTENT PER 100 GM. OF FOOD		
	Calcium	Magnesium	Phosphorus
	mg.	mg.	mg.
Cannon diet (low Mg.)	440	69	251
Cannon diet with added Mg.	440	206	251
Purina fox chow	1600	272	1000

TABLE 2. *Summary of urine findings on different diets*

DIET	VOLUME	pH	CALCIUM	MAGNESIUM	PHOSPHORUS
	cc/day		mg. %	mg. %	mg. %
Cannon (low Mg.)	8.5	6.42	24.3	20.5	289
Cannon with added Mg.	11.9	6.23	28.4	57.9	251
Purina fox chow	14.8	6.30	29.6	41.4	142
Purina fox chow +10% basaljel	15.9	7.06	27.4	35.3	49

Experiment 2. Prevention of stone by reducing the urinary phosphorus. It has been shown that certain aluminum gels, by forming insoluble aluminum salts with the available phosphate in the gastro-intestinal tract, lead to a reduction of the phosphate excreted in the urine.[5] Because of this action aluminum gels

have been recommended as prophylactic therapy in cases of phosphatic urinary calculi.[6,7] To test the efficacy of aluminum gel on rat calculi, an experiment was devised using the preparation called basaljel, a material composed of basic aluminum carbonate. Two groups of rats were used. One received the control diet of Purina fox chow while the other was fed a diet composed of a mixture of 90 parts fox chow and 10 parts basaljel. Even with such a large intake of basaljel, the diet was apparently quite palatable. The rats ate it readily and remained in good nutrition for the duration of the experiment.

---

[5] Freeman, S. and Freeman, W. M. C.: Phosphorus retention with chronic renal insufficiency: Effect of diet and the ingestion of aluminum hydroxide. Am. J. Dis. Child. 61: 981, 1941.

Table 2 shows the urinary changes that occurred with basaljel. The phosphorus concentration in the urine was depressed to one third the control level. It may be noted also that the urinary pH was distinctly elevated. In table 4 the average weight of stone produced in the two groups is compared. Basaljel was found quite effective in preventing stones during the 6 weeks of the experiment.

TABLE 3. *Exp. 1. Prevention of stone by diet low in magnesium*

DIET GROUPS	NUMBER OF RATS IN GROUP	AVER. CONC. MAGNESIUM IN URINE	AVER. WEIGHT OF STONE PRODUCED IN 6 WEEKS
		mg /100 cc	mg.
Cannon (low Mg.)	30	20.5	7.7 ± 2.8*
Cannon with added Mg.	16	57.9	61.7 ± 13.8
Purina fox chow	29	41.4	50.6 ± 10.9

Statistical comparison:
Stone weight Cannon vs. Cannon plus Mg.
$t = 5.025$
* Standard Error

TABLE 4. *Exp. 2. Prevention of stone by reducing urinary phosphorus*

DIET GROUPS	NUMBER OF RATS IN GROUP	AVER. CONC PHOSPHORUS IN URINE	AVER. WEIGHT OF STONE PRODUCED IN 6 WEEKS
		mg./100 cc	mg.
Purina fox chow	24	142	72.4 ± 17.5*
Purina fox chow +10% basaljel	24	49	9.9 ± 4.5

Statistical comparison:
Stone weight—$t = 3.44$
* Standard Error

Experiment 3. Dissolution of stones by low magnesium diet and by basaljel. The same general methods for testing dissolution were used in this experiment as have been reported in previous papers. Foreign body stones were first developed in the bladders of rats by feeding them the standard diet of fox chow checkers. At the completion of the stone-growing period, the animals were operated upon and the stones were extracted, weighed, and immediately replaced. In the instances where stone had not formed the animals were discarded. The remaining

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[6] Shorr, E.: Possible usefulness of estrogens and aluminum hydroxide gels in management of renal stone. J. Urol., **53:** 507, 1945.

[7] Shorr, E. and Carter, A. C.: Aluminum gels in the management of renal phosphatic calculi. J.A.M.A., **144:** 1549, 1950.

animals, each with a stone in the bladder, were divided into three groups. One group continued on the control diet of Purina fox chow. The second group was given the Cannon diet to see if a diet low in magnesium resulted in dissolution. The third group was fed fox chow with 10 per cent basaljel. Four weeks later the animals of all three groups were killed. Table 5 shows the results obtained. As has been demonstrated in similar experiments previously, the stones in the control group continued to grow. On the other hand, the group that received the Cannon diet (low magnesium) showed marked stone dissolution. In nine of the eleven cases complete dissolution occurred. The results with basaljel, however, were somewhat disappointing. Of the 32 stones in this group, 9 stones instead of dissolving showed some increase in weight, the maximum increase being 63 mg. Only 4 stones of the entire group dissolved completely (76, 72, 62, and 35 mg.). The remaining 19 stones were either unchanged or incompletely dissolved. The average weight change was a loss of 16 mg. for the entire group.

TABLE 5. *Exp. 3. Dissolution of calculi by low magnesium diet or by basaljel*

NUMBER OF RATS IN GROUP	AVERAGE INITIAL STONE WT.	DIETARY TREATMENT FOR 4 WEEKS	AVERAGE CHANGE IN STONE WT.
	mg.		mg.
30	82.1	Control—fox chow	+55.6
11	79.6	Cannon (low Mg.)	−59.9
32	91.7	Fox chow + basaljel	−16.3

Statistical comparison: stone weight change:
Control vs. Cannon t = 4.826
Control vs. Basaljel t = 4.982

DISCUSSION

These experiments illustrate the fundamental importance in urolithiasis of the urinary concentration of the poorly soluble crystalloids. By increasing or decreasing the concentration of individual ions it was possible to induce or prevent the development of a calculus containing these ions. This is neither surprising nor new. It is widely accepted that precipitation from a saturated or supersaturated urine is intimately related to the process of stone formation and, of course, a precipitate is encouraged by an increased concentration of any of its component ions. The conditions favoring precipitation are not, however, the only controlling factors in stone formation, for a precipitate can lead to stone only if some of the precipitated material is retained in the urinary system. Accordingly, circumstances that predispose to retention become important. Most, if not all, of the known causes of stone will fall in one or the other of these two fundamental categories: either they favor precipitation or they favor retention of precipitate. Conditions causing retention may, in turn, be divided into abnormalities producing stasis and abnormalities producing a foreign surface where the precipitate adheres. It must be admitted that a stone is not simply a disorganized aggregate of retained precipitate, for the crystalloid in a stone is laid down in an organized pattern. However, the physico-chemical processes that lead to such organization are, insofar as urinary calculi are concerned, almost entirely speculative at the present time.

In all our rats a condition favoring retention of precipitate was present by virtue of the foreign body in the bladder. Stone formation depended upon the occurrence of precipitation from the urine, and precipitation was controlled by increasing or decreasing the concentration of the constituent ions of the precipitable compound. It must be remembered that the total concentration of a chemical radical as determined by analysis of the urine does not necessarily indicate the actual concentration of that ion free in solution. This is especially the case with the phosphate radical because of its ability to form more complex ions of mono- and di-hydrogen phosphate. In the rats fed the Cannon diet the concentration of magnesium in the urine was low but the concentration of phosphate was very high. One might expect that the high phosphate would offset the low magnesium and that stones would form on such a diet. Actually, no stones formed, presumably because the concentration of phosphate ions did not increase in proportion to the increase in the total phosphate present. It should be stated that in the experiments given in this paper, determinations of the ammonium present in the urine were not made. Yet, since the ammonium ion enters into the composition of the stone, its concentration is of importance equal to that of magnesium or phosphate in determining whether or not precipitation occurs according to the solubility-product principle.

Some comment should be made on our results with basaljel. Considerable amounts of phosphorus were still excreted in the urine of the rats even though the dose of basaljel was very large, corresponding to approximately 500 cc per day for a man weighing 70 kg. In the rats the urinary phosphorus was reduced to one-third the control level, while Shorr and Carter[7] found in human patients that relatively much smaller doses resulted in a 6 to 8-fold reduction in the phosphorus excretion. We have made a few observations of the effect of basaljel on human beings. We used a diet much higher in phosphorus than the diet used by Shorr and Carter,[7] who limited their patients to approximately 1200 mg. of phosphorus per day. In the few observations that we have made, the reduction in phosphorus excretion by treatment with basaljel has been rather disappointing. We used patients with neurologic disease who had been completely tube-fed for some time, so that it was possible to rigidly control the food intake. During the initial control period of 6 days, and the experimental period of 6 days that followed it, the food intake was kept constant except that 160 cc basaljel was mixed with the feeding formula each day of the experimental period. The phosphorus intake was 4.8 gm. per day. Urine collections were made for the last 3 days of each period. In experiments on 3 patients the average phosphorus excretion was reduced from 1079 mg. per day in the first period to 777 mg. per day in the basaljel period. It would seem from this result that the recommended daily dose of 160 cc basaljel will not significantly reduce the urinary phosphorus when the phosphorus content of the food is high.

SUMMARY

In experiments on the formation of magnesium ammonium phosphate calculi in rats, it was found that calculi could be prevented by reducing the concentration in the urine of either the magnesium or the phosphate. Reduction of magnesium in the urine was accomplished by reducing the magnesium in the diet. Phosphate excretion was reduced by feeding large amounts of basaljel, a gel of basic aluminum carbonate. Other experiments showed that stones previously formed could be dissolved in many instances by the same measures. The validity of these conclusions is affirmed in each experiment by application of the statistical "t-test". The experiments support the use of basaljel in human cases of phosphate urolithiasis.

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SUMMARY

In experiments on the formation of magnesium ammonium phosphate calculi in rats, it was found that calculi could be prevented by reducing the concentration in the urine of either the magnesium or the phosphate. Reduction of magnesium in the urine was accomplished by reducing the magnesium in the diet. Phosphate excretion was reduced by feeding large amounts of basaljel, a gel of basic aluminum carbonate. Other experiments showed that stones previously formed could be dissolved in many instances by the same measures. The validity of these conclusions is affirmed in each experiment by application of the statistical "t-test". The experiments support the use of basaljel in human cases of phosphate urolithiasis.

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THE RELATIONSHIP BETWEEN ALKALINE PHOSPHATASE IN THE KIDNEY AND URINARY CALCULI

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A great deal of fundamental information concerning the mechanism of the formation of urinary calculi has been presented by Higgins, Keyser, Randall, and many others. However, the exact biochemical processes involved in stone formation in the kidney remain to some extent an unsolved problem.

Since the discovery of alkaline phosphatase in the intestinal mucosa, and its abundance in the kidney as shown by Gomori,[1] the relationship of this enzyme to renal calcification has been studied by several investigators. One of the functions of alkaline phosphatase is to decompose organic phosphorous compounds into inorganic phosphate, usually in the form of calcium phosphate. In addition to being present in the kidney, it is widely distributed in ossifying cartilage and bone.

In 1932 Harris[2] pointed out the tendency to calcification in the kidney, and other organs rich in alkaline phosphatase. Breedis, Flory, and Furth[3] made extensive studies of alkaline phosphatase levels in the urine in relation to renal injury. They found that in both rats and rabbits, following the injection of uranium nitrate, there was a sharp rise in both the total amount of alkaline phosphatase excreted in the urine, and in the concentration of that enzyme in the tubular epithelium. Their conclusion following Gomori stains was that the rise in the alkaline phosphatase content of the urine was caused by the excretion of necrotizing phosphatase rich cells of the proximal convoluted tubules. In rats which died 6 days after injection of uranium nitrate, renal calcification was found along with many phosphatase containing casts. They also noted that calcification first took place in the cellular and granular casts rich in phosphatase. However, Hepler and Simonds[4] studied the relationship of calcification and the existence of alkaline phosphatase by producing renal necrosis with nephrotoxic poisons, and concluded that phosphatase was not concerned with calcification in the kidneys of dogs. In their opinion, the presence of fat in the proximal convoluted tubules was the principal factor in the deposition of calcium.

In view of the various conflicting reports, it was believed that it would be of value to produce calculi in rabbits and rats and study the phosphatase activity in those kidneys in which calculi were found, both by biochemical and histological methods. Therefore, the study resolved itself into two phases:

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[1] Gomori, G.: Distribution of phosphatase in normal organs and tissues. J. Cell. and Comp. Physiol., **17**: 71–83, 1941.

[2] Harris, L. J.: The mode of action of vitamin D. The "parathyroid" theory: Clinical hypervitaminosis. Lancet **1**: 1031–1038, 1932.

[3] Breedis, C., Flory, C. M. and Furth, J.: Alkaline phosphatase level in urine in relation to renal injury. Arch. Path., **36**: 402–412, 1943.

[4] Hepler, O. E. and Simonds, J. P.: Experimental nephropathies; calcification and phosphatase in kidneys of dogs poisoned with mercury bichloride, potassium dichromate, and uranyl nitrate. Arch. Path., **40**: 37–43, 1945.

1) The production of calculi in rabbits by oral feeding of oxamide, with and without ureteral obstruction, and the determination of alkaline phosphatase in the renal tissue both by chemical analysis and the Gomori technique.

2) The production of urinary calculi in albino rats by a diet deficient in vitamin A, but adequate in every other respect, with alkaline phosphatase studies on renal tissue.

The method used to produce calculi in rabbits was that described by Keyser.[5] Ten full grown rabbits were fed two 0.4 gm. oxamide capsules daily from 53 to 75 days, with 8 rabbits being used as controls. There was no attempt to restrict water from these animals, and all were fed on a balanced stock laboratory diet.

The upper left ureter was partially occluded by rubber bands or catgut loosely tied about the ureter in six of the animals on oxamide. No operative procedure was carried out on the other four. No significant change of serum phosphatase was noted in any animal following the administration of oxamide. At the conclusion of the study all animals, including controls, were sacrificed and a careful search made for calculi in the urinary tract of each. Gomori stains were made on each kidney. In addition, tissue extracts were made from each kidney, and the results expressed as units of phosphatase present in 1 gm. of tissue extracted in 100 cc of normal saline are tabulated in table 1.

Of the 6 rabbits subjected to operative obstructive procedures on the left ureter, four showed a marked left hydronephrosis, and two developed atrophic left kidneys. Only one of the six was found to have calculi in the kidney pelvis. Another with an atrophic left kidney had fine yellow sand in the bladder. Two of the rabbits receiving oxamide, but with no obstructive procedure on either ureter, were found to have sand in the kidney pelvis and bladder. One of the latter had four 3 by 4 mm. calculi in the left kidney. None of the controls developed calculi.

Phosphatase determinations on the atrophic or hydronephrotic kidneys were either markedly decreased or too low to read by the method used. This finding was further confirmed by stains made with the Gomori technique (fig. 1). In this section one notes an extensive degeneration of tubular elements, with marked replacement by fibrous tissue. In addition, there is an almost complete absence of stainable phosphatase. This finding confirms earlier observations by Wilmer.[6] It is noteworthy that in experimental animal number 80, in whom sand was found in the left kidney and bladder, the phosphatase determination was too low to be determined on the affected kidney, and Gomori stains show a complete absence of the enzyme. In the unobstructed rabbit kidney, where calculi were present, there appeared to be a moderate reduction of alkaline phosphatase as noted on the Gomori stain, in comparison with the normal control (figs. 2 and 3). This impression was substantiated by a comparison of the average phosphatase per 100 cc in the kidneys in which no calculi were found, including

[5] Keyser, L. D.: The etiology of urinary lithiasis: An experimental study. Arch. Surg. **6**: 525–553, 1923.

[6] Wilmer, H. A.: Renal phosphatase; correlation between functional activity of renal tubule and its phosphatase content. Arch. Path., **37**: 227–237, 1944.

both the controls and those on oxamide, with those kidneys in which calculi were found. The average was .62 units for those without calculi and .39 units for those with calculi. It is realized that this number is not sufficient to form any definite conclusion, but there appears to be a definite correlation between the tissue extract and the Gomori stains, which would tend to support this conclusion.

TABLE 1. *Experimental production of urinary calculi in rabbits*

RABBIT	URETERAL OBSTRUCTION	DAYS ON OXAMIDE	AVERAGE SERUM PHOSPHATASE		AVERAGE RENAL PHOSPHATASE		URINARY TRACT CALCIFICATION
			Preoperative	Post Oxamide	Right	Left	
					gm./100 cc	*gm./100 cc*	
95	Control	0	3.82 B.U.	Control	0.98	0.53	None
77	Control	0	5.46 B.U.	Control	0.41	0.53	None
35	Control	0	3.05 B.U.	Control	—	—	None; died of many abscesses
79	Control	0	4.05 B.U.	Control	0.85	1.58	None
45	Control	0	3.92 B.U.	Control	0.47	0.55	None
50	Control	0	5.63 B.U.	Control	0.52	0.49	None
100	Control	0	3.02 B.U.	Control	0.39	0.54	None
78	Control	0	2.32 B.U.	Control	—	—	Died; causes unknown
85	With rubber band	3	— B.U.	2.43 B.U.	0.12	0.06	No calcification; left hydronephrosis
44	With rubber band	75	1.45 B.U.	1.24 B.U.	0.28	Too low	No calcification; left hydronephrosis
80	Catgut	60	3.26 B.U.	5.82 B.U.	1.03	Too low	Sand, left kidney and bladder; left hydronephrosis
81	Catgut	60	2.79 B.U.	3.90 B.U.	2.01	Too low	No calcification; left hydronephrosis
82	Catgut	53	1.80 B.U.	5.72 B.U.	0.31	Too low	No calcification; atrophic left kidney
84	Catgut	75	3.15 B.U.	1.58 B.U.	0.40	Too low	Sand, bladder; atrophic left kidney
88	None	58	7.27 B.U.	— B.U.	0.28	0.22	Sand, both kidneys; 3 by 4 mm. calculus, left kidney
87	None	53	5.20 B.U.	6.28 B.U.	0.48	0.65	No calcification
91	None	53	2.92 B.U.	4.02 B.U.	0.17	0.24	No calcification; kidneys and bladder normal
39	None	53	2.55 B.U.	2.98 B.U.	0.66	0.38	Sand, both kidneys and bladder

Twenty albino rats were used for the experiment in which a vitamin A free diet was used. Five rats were used as controls and fifteen were fed on a diet similar to the one used by Bliss, Livermore and Prather[7] in their experiment. The rats were maintained on this diet for from 93 to 152 days and then sacri-

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[7] Bliss, A. R., Jr., Livermore, G. R. and Prather, E. O., Jr.: Relation of vitamin A and vitamin D to urinary calculus formation. J. Urol., 30: 639–652, 1933.

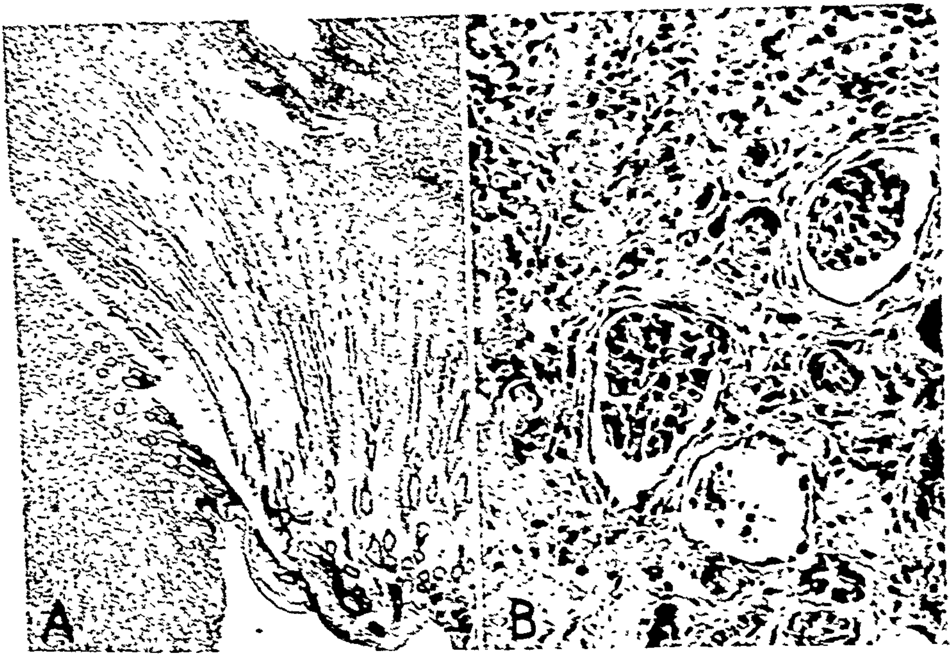

FIG. 1. *A*, low power. *B*, high power. Rabbit No. 80. Hydronephrosis. Sand in left kidney pelvis. Catgut around upper ureter. Gomori stain. Almost complete loss of tubular structures with extensive fibrosis. Almost complete absence of alkaline phosphatase.

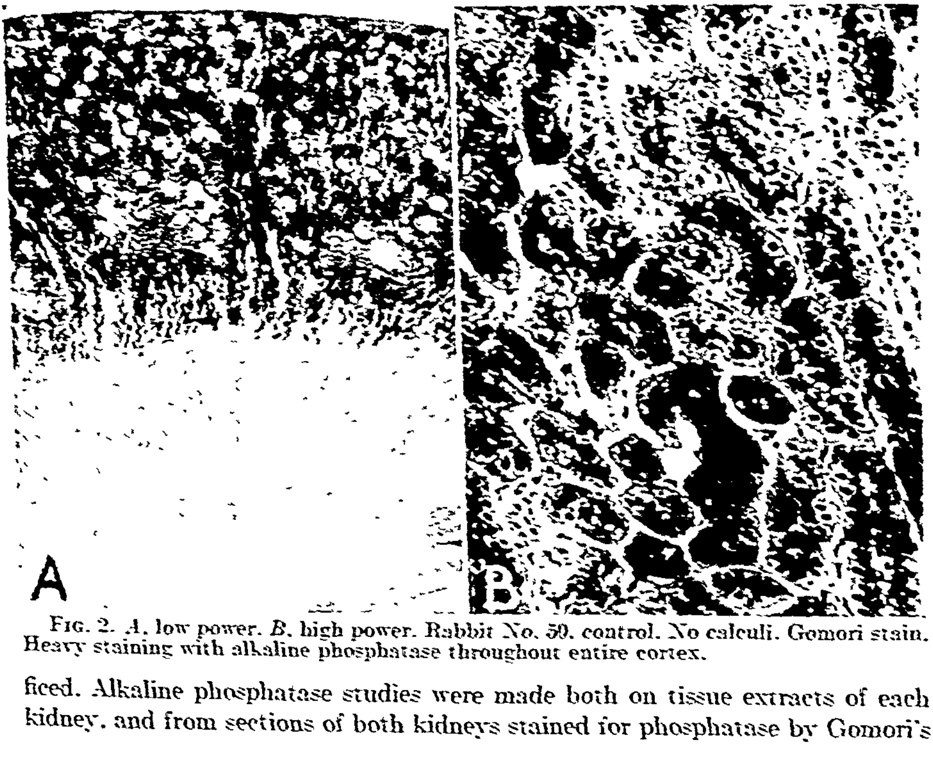

FIG. 2. *A*, low power. *B*, high power. Rabbit No. 50, control. No calculi. Gomori stain. Heavy staining with alkaline phosphatase throughout entire cortex.

ficed. Alkaline phosphatase studies were made both on tissue extracts of each kidney, and from sections of both kidneys stained for phosphatase by Gomori's

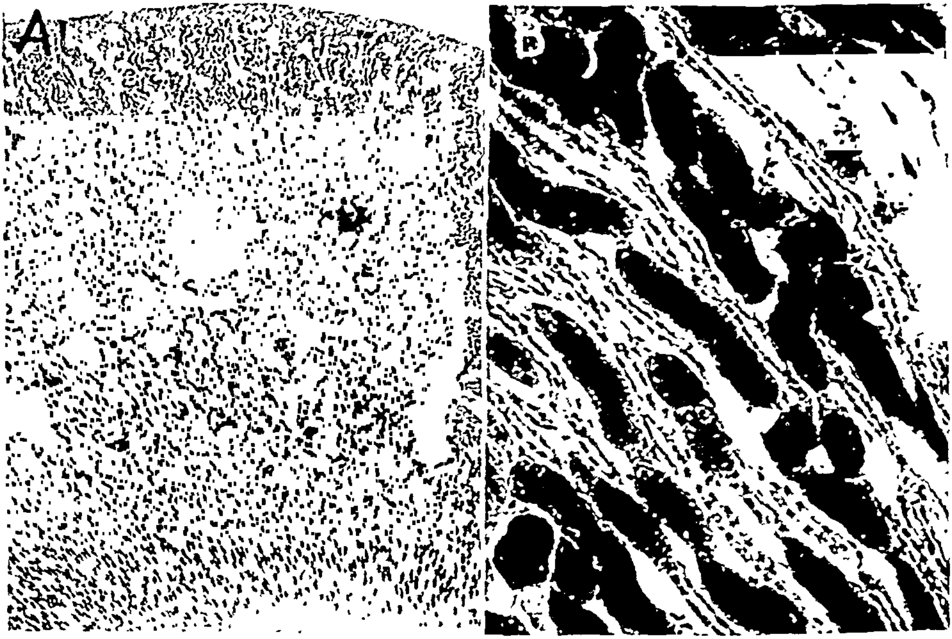

Fig. 3. *A*, low power. *B*, high power. Rabbit No. 39. Sand in both kidneys and bladder. Gomori stain. Although cortex is wider than in figure 2, there is actually less dense staining. Considerable intratubular alkaline phosphatase noted in higher power.

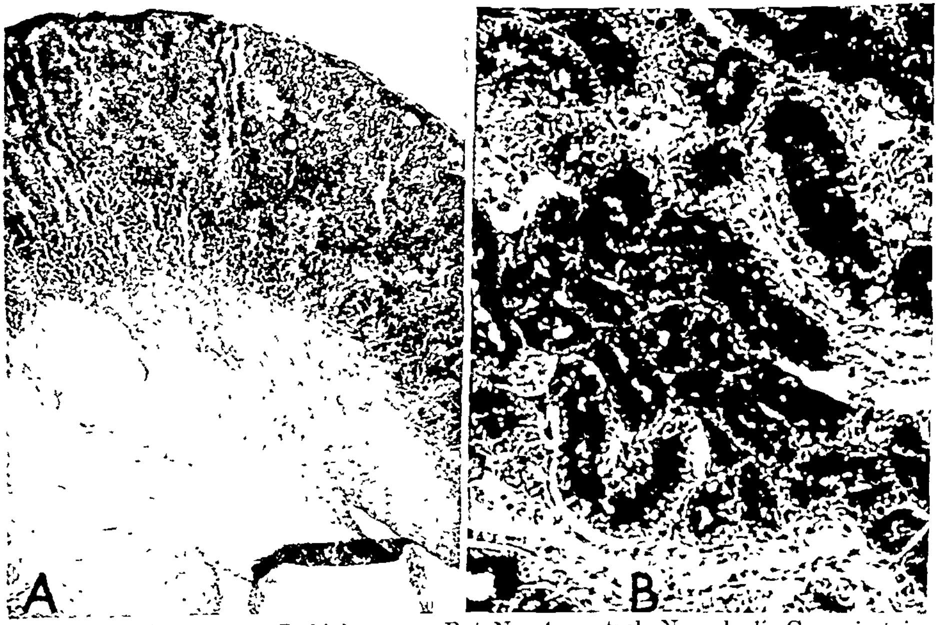

Fig. 4. *A*, low power. *B*, high power. Rat No. 4, control. No calculi. Gomori stain. Heavy Tubular staining.

method. A careful search was made for calculi in the urinary tract. Results are recorded in table 2.

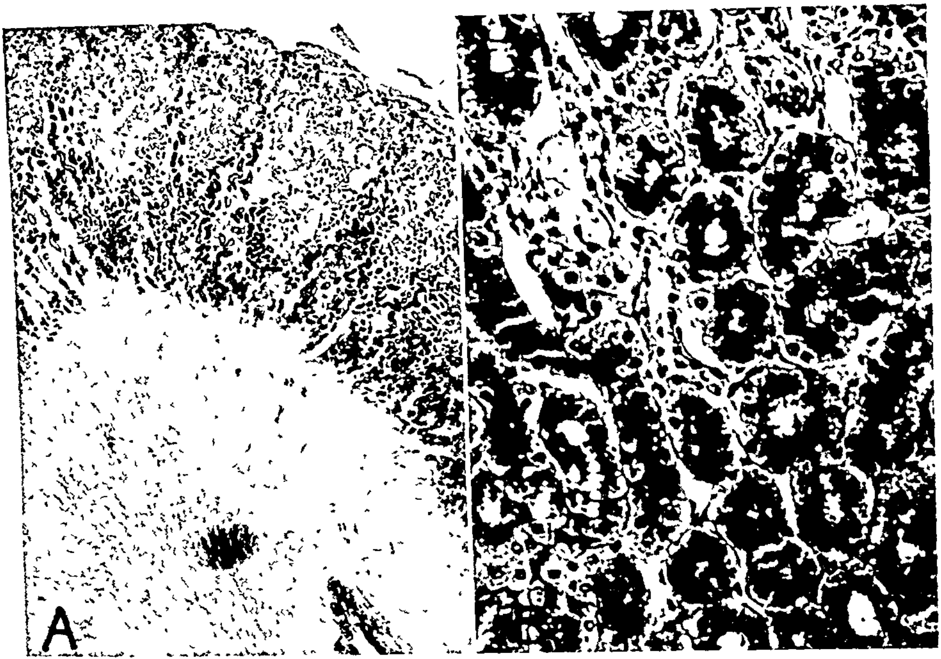

FIG. 5. *A*, low power. *B*, high power. Rat No. 12. Soft sand, both kidney pelves. Gomori stain. Definite decrease in alkaline phosphatase compared to figure 4.

TABLE 2. *Experimental production of urinary calculi in rats with avitamin A diets*

RATS	DAYS ON DIET	AVERAGE RENAL PHOSPHATASE*		URINARY TRACT CALCIFICATIONS
		Right	Left	
		gm/20 cc	*gm/20 cc*	
1	Control	6.5	6.48	No calcification
2	Control	6.6	8.8	No calcification
3	Control	2.40	3.4	No calcification
4	Control	4.98	8.50	No calcification
5	Control	5.40	5.18	No calcification
6	93	3.06	4 24	Rat pregnant; no calcification
7	93	3.01	2.50	No calcification
8	143	2.81	2.33	No calcification
9	143	4.54	4.30	Fine yellow sand in right pelvis; left normal
10	152	1.66	1.95	Stones, both pelves; 2 mm. diameter, white
11	152	2.40	4.40	Stones, both pelves; 3 by 3 diameter
12	152	7.46	5.48	Soft sand, both pelves
13	152	3.48	3.91	Stone on right papilla
14	152	2.61	—	Fleck of calcification in right pelvis
15	152	4.13	4.18	Sand and calcification both pelves

* Units of phosphatase expressed as units of phosphatase released from 1 gm. tissue extracted with 20 cc extracting fluid.

Seventy per cent of the rats developed calculi in the urinary tract. Five of the animals died during the experiment. Calculi in various stages of formation were found, ranging from fine sand to well developed calculi. No calculi were found before 143 days and none were present in the control animals. Although an analysis of tissue determinations showed an alkaline phosphatase average of 5.8 units for the control rats and 3.96 units for those developing renal calculi, an examination of individual determinations revealed considerable variation in the range of phosphatase both in the rats with calculi and in those where none occurred. There was also a wide variation in the Gomori stains. However, in general there seemed to be a suggestive decrease in alkaline phosphatase in those kidneys where calculi were present (figs. 4 and 5).

No explanation for the apparent decrease in alkaline phosphatase is readily apparent. In the rabbits, the decrease was probably secondary to the prolonged administration of a nephrotoxic substance, oxamide. Perhaps nutritional factors accounted for the decrease in the rats. In any event, there was definitely no increase in phosphatase such as would be necessary if this enzyme was a contributory factor in the production of calculi.

SUMMARY

Rabbits maintained on oxamide with and without ureteral obstruction developed urinary calculi.

In kidneys with hydronephrosis or atrophy, there was an almost complete loss of alkaline phosphatase. Calculi developed in one of these kidneys.

Albino rats maintained on a vitamin A deficient diet developed urinary calculi in about 70 per cent of the cases.

No definite connection between the amount of alkaline phosphatase present and the formation of renal calculi was observed in either rabbits or rats. However, there seemed to be a decrease in alkaline phosphatase in those kidneys where calculi developed.

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RENAL HEMODYNAMICS IN CLINICAL UROLOGY

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The role of renal physiology and function studies as an integral part of daily urological practice has been a secondary one. The clinical urologist has always had his indications for surgery: obstruction, infection, stone, tumor, and congenital anomalies have been the usual reasons for operative intervention. Ever mindful and yet rather neglectful of the role of renal function, the urologist has adhered somewhat tenaciously to the above listed tenets of surgical indications. Today, the routine urinalysis, the blood urea nitrogen, the excretory urogram, and on occasion phenolsulfonthalein excretions have comprised the gamut of function tests for the urologist. However well these tests have served him, the need for other more accurate, more quantitative, more sensitive tests of renal function is ever present. The over-all purpose of this work is, in essence, an attempt to correlate modern quantitative biochemical tests of renal function with everyday clinical urological problems.

One of the important steps requisite to the advancement of renal function technique was the development of methods of measurement of the urea nitrogen. Urea nitrate crystals, described by Schmidt in 1846, were simply weighed at first. The later development of the mercuric oxide titration method of Leibig and the carbon dioxide method of Bunsen were definite forward steps. In 1883 Kjeldahl described his method for the determination of nitrogen.

Accumulation of such nitrogenous waste products with resultant elevation of the blood urea nitrogen was one test indicative of kidney failure. Austin, Stillman, and van Slyke introduced the urea clearance test in 1921. Subsequent improvements in technique and apparatus by van Slyke and Maclean have followed and have helped to make possible some of the more recent developments in the realm of renal function.

Renal clearance methods first applied to urea were next extended to a study of the excretion of other materials in a further attempt to understand the normal and the diseased kidney. Inulin, mannitol, glucose, diodrast, sodium para-amino hippurate and sodium thiosulphate have been the principal substances utilized in the development of clearance techniques. These more recent developments culminating in the monumental work of Homer Smith and his associates form a background for the work to be presented.

PURPOSE

The numerous contributions of Homer Smith, James Shannon, Robert Pitts and their associates undoubtedly comprise the cornerstone upon which much of modern renal physiology rests. This paper is partly based upon the methods of Smith and his colleagues which permit simultaneous measurement of the glomerular filtration rate and the renal plasma flow. Many of the problems confronting the urologist regarding kidney function have had to go unanswered mainly because of a lack of method of study. Although many clinical applications of the renal clearance studies of Homer Smith have been made, almost none have been made with the "surgical" kidney.

Utilizing the procedures of Smith and his associates, a study of renal function was begun with several clinical urological problems in mind:

1) The first purpose was a general study of the functional patterns of the surgical kidneys. Those involved by varying types of calculus disease, tuberculosis, tumor, hydronephrosis, pyelonephritis, renal ischemia, and infarction, were studied and compared with the normal. In addition, the horseshoe and polycystic kidney, as well as the kidney subjected to heminephrectomy, were studied.

2) The second purpose concerns a study of the problem of compensatory hypertrophy and of physiological effects of nephrectomy upon function of the remaining kidney.

3) Finally an investigation of the problem of reflex anuria was begun in the dog utilizing these same clearance and extraction techniques. The purpose of this particular phase of the investigation was to introduce a new method of study rather than to present definitive results.

METHODS

The clearance procedures introduced by Homer Smith and associates permitting simultaneous measurement of glomerular filtration rate and effective renal plasma flow, have been utilized in this clinical and experimental work in which 107 determinations were performed in 16 subjects and 4 dogs.

Glomerular filtration rate (GFR) has been determined by thiosulphate clearance. Thiosulphate was measured in Folin Wu filtrates of plasma and in samples of urine using methods described by Elliott Newman. Newman has found clear ances of inulin and thiosulphate to be identical and he therefore concluded that the latter was an accurate measurement of the GFR. It has also been established that thiosulphate clearance causes no change in the para-amino hippurate clearance utilized in the measurement of the effective renal plasma flow.

Effective renal plasma flow (RPF) was determined by para-amino hippurate (PAH) clearances at low plasma concentrations. PAH was measured in cadmium filtrates of plasma and in dilute urine samples uring the methods of Goldring and Chasis. From the RPF renal blood flow (RBF) was calculated using the venous hematocrit index:

$$\text{RBF equals RPF times } \frac{100}{100 \text{ minus hematocrit}}$$

Filtration fraction (FF) defines the proportion of water filtered by a unit of plasma flow and varies with filtration pressure. FF was calculated as follows:

$$\text{FF equals } \frac{\text{GFR}}{\text{RPF}}$$

Brachial blood pressure readings were obtained during the course of the clearance periods. The arithmetic mean of systolic and diastolic pressures (Pm) was used in the calculation of total crude renal resistance (RR) as follows:

$$\text{RR equals } \frac{\text{Pm}}{\text{RBF}}$$

This figure represents total crude renal arterial arteriolar resistance. Lamport's procedure of calculating apparent renal vascular resistance is probably more accurate and expresses the sum of the afferent (Ra) and efferent (Re) arteriolar resistance. The more rough estimate obtained as described is sufficient for the purposes intended within the scope of this paper.

The aforementioned data, direct and calculated, were obtained in each of the experiments to be described. In some of the patients, bladder urine was used in the calculations, while in others, individual specimens were collected from both kidneys. Bulb type ureteral catheters measuring 6F to 10F were used and the positions in the ureters were checked by x-ray. The bladder was then examined in those undergoing ureteral catheterization to be certain that no urine had leaked around the catheters during the tests.

Clearances were run under standard conditions. Meals were withheld and the subject was given approximately 24 ounces of water before the beginning of clearance periods. The infusion of thiosulphate and PAH was given in normal saline in one antecubital vein at the rate of 60 to 80 drops per minute, while blood pressure readings and blood samples were taken from the opposite arm; heparin was used as anticoagulant. The catheter utilized in the collection of the bladder was firm with more than the usual number of openings. After injection of a priming dose of both thiosulphate and PAH, twenty minutes were allowed to elapse before beginning the clearance periods. Then, two to four 15 to 20 minute periods were run in each patient.

In patients in whom extraction ratios of PAH were determined, the technique of right auricular catheterization developed by Forssman and modified by Cournand was utilized. Under fluoroscopic control the catheter was passed through the right auricle into the inferior vena cava and into the renal vein. Samples were then taken from the renal vein and from the femoral artery, and the extraction ratio of PAH by each kidney was determined.

In the normal human Bradley and his co-workers have found the average extraction ration of PAH to be 92 per cent, ranging from 87.5 per cent to 100 per cent. The figures are slightly lower in the left renal vein because of the mixture of blood from the left spermatic or ovarian vein.

Normal human clearance patterns are shown in table 1 which was tabulated from collected data from the literature.

Shock has demonstrated a decrease in renal function with advancing age. Table 2 is reprinted from the unpublished work of Shock.

After a comparison of tables 1 and 2 is made, it can be readily seen that the clearances depicted in table 1 are those of young adults. These figures are of special significance in this particular group of patients studied in that the middle and older age group subjects were utilized for the most part.

Animal methods. Dogs were used whose weights varied between 18 and 37 pounds. Food was withheld on the morning of the experiment. Except for this no special effort was made to regulate degree of hydration.

Intraperitoneal veterinary nembutal was used for anesthesia (1 cc per 5 pounds of body weight). In two instances additional ether was necessary. The neck as well as the abdomen was shaved, cleaned, and prepared for surgery. Sterile technique was utilized and all dogs survived to be used for additional experiments.

TABLE 1. *Normal human clearance patterns*

	GFR	RPF	RBF	FF
	cc per 1.73 sq.m./min.			
Human male	110–153	563–831	1400	.18
Human female	101–133	492–696	1200	

In the calculation of RBF 700 was taken as average RPF in the male and in the female.

Hematocrit was taken at 50.

Surface area was calculated by the Meeh-Rubner equation:

$$\frac{\text{Surface area in sq.m. equals } 11 \times 2 \text{ times } 2/3W}{100}, \text{ where W is body weight in kilograms.}$$

TABLE 2. *Renal clearance pattern changes with advancing age*

AGE	GFR	RPF
	cc per 1.73 sq.m /min.	
20	122.8	613.0
30	115.0	649.3
40	121.2	573.8
50	99.3	500 8
60	96.0	442.1
70	89.0	354.0
80	65.3	288.0

An external jugular vein was used for continuous infusion. Sodium thiosulfate and PAH were used for clearances in determination of glomerular filtration rate and effective renal plasma flow respectively. An opposite external jugular vein was used to collect blood samples.

Because the very essence of one of the experiments was to determine the effects of urethral dilatation and transurethral prostatectomy upon glomerular filtration rate and effective renal plasma flow, it was necessary to obtain urine without going through the urethra. Suprapubic cystotomy was therefore performed. A No. 6 ureteral catheter was then inserted midway up the right ureter through the opened bladder. As the urine was seen to flow freely from the ureteral catheter and three control clearance periods were run, the urethra was then dilated to 16F by way of the cystotomy opening and an additional clearance period was then run. Following this a resection of the bladder neck to simulate as closely as possible a transurethral prostatectomy was carried out. During the process of the dilatation and the "prostatectomy" clearance periods were determined utilizing urine from the ureteral catheter inserted through the suprapubic cystotomy incision.

In two animals extraction ratios of PAH were determined in an attempt to further study this problem. Since it was not possible to catheterize the renal vein by way of the heart, as done in two of the human subjects previously described, it was necessary to expose the renal pedicle and the adjacent aorta. Samples of blood were then withdrawn from the right renal vein and from the aorta. The ability of the kidney to extract PAH was next determined. After two extraction periods the urethra was vigorously dilated to 18F. This is a fair degree of dilatation when one considers the fact that male dogs were used. Following this an additional extraction period was run to determine the effects of urethral dilatation.

RESULTS

Effect of nephrectomy for unilateral kidney disease upon glomerular filtration rate and effective renal plasma flow in the remaining kidney. Five patients with unilateral kidney disease who have undergone nephrectomy and 1 patient with an hydronephrotic autonephrectomy resulting from an obstructing stone at the ureteropelvic junction were selected for study. GFR and RPF were determined preoperatively and postoperatively in the healthy and in the diseased kidney in 3 patients, thereby establishing renal clearance patterns for the particular disease under consideration. Repeat clearances were then determined in the remaining kidney postoperatively thereby noting effects of nephrectomy upon function of the remaining mate. In 2 patients renal clearances were determined at stated intervals postoperatively, thereby measuring progressive changes in function in the remaining kidney following nephrectomy. The findings are seen in table 3.

Case N. F. M., a 27 year old normotensive colored female nurse had right renal tuberculosis limited to the upper major calyx. Right kidney urine was guinea pig positive for acid-fast bacilli, while urine from the left kidney was negative. Urine remained guinea pig positive despite 5 weeks of streptomycin therapy so that right nephrectomy was performed on May 10, 1949. Four months later the patient was asymptomatic and urine was normal. At this time, as seen in table 3, GFR in the remaining left kidney had more than doubled (43.19 to 92.7) and effective RPF had shown a definite increase (270 to 379).

Case A. M. The severity of the tuberculous process in this patient can be seen from table 3 when the GFR and effective RPF are compared with those figures of the previous patient. Urine from the right kidney was guinea pig positive for acid-fast bacilli while the left kidney urine was normal. Streptomycin was given preoperatively for several weeks and right nephrectomy was performed on November 23, 1948. Several weeks later the patient had a recur-

TABLE 3. *Effects of nephrectomy upon glomerular filtration rate and effective renal plasma flow in remaining kidney*

PATIENT	SEX	AGE	DIAGNOSIS	OPERATION	DATE OF OPERATION	DATE OF CLEARANCES	TIME DAYS POST-OPERATIVE	SOURCE OF URINE			GFR	RPF	RBF	AVERAGE			
								Right Kidney	Left Kidney	Bladder	cc per 1.73 sq.m./min.			FF	B.P.	Pm	RR
N. F. M.	F	27	Early right renal tuberculosis			May 5, 1949		x			32.55	207	315	.15			.26
									x		43.19	270	450	.16	110/70	90	.20
				Right nephrectomy	May 10, 1949												
						Sept. 29, 1949	145			x	92.7	379	665	.24	121/77	99	.15
A. M.	F	36	Advanced right renal tuberculosis			Nov. 18, 1948		x			4.0	22.8	41.0	.13			.22
									x		59.2	328	585	.18	108/25	91	.15
				Right nephrectomy	Nov. 23, 1948												
						Aug. 29, 1949	261			x	87.5	402	758.4	.21	111/78	95	.12
L. W. W.	M	56	Left renal calculi			June 20, 1949		x			39.3	230	327	.12			.27
									x		48.6	307	503	.15	124/82	103	.20
				Left nephrectomy	June 21, 1949												
						Aug. 29, 1949	68			x	53.6	267	430	.20	123/90	107	.25

T. M.	M	60	Right renal calculus	Right nephrectomy	Dec. 11, 1918												
						Dec. 28, 1918	11			x	00.0	251	401	.21	122/76	90	.21
						Jan. 3, 1919	21			x	80.7	370	713.1	.21	118/70	90	.13
						Feb. 7, 1919	20			x	80.2	410	785.7	.20	117/78	97	.12
G.	M	51	Right infected hydronephrosis	Right nephroureterectomy	Aug. 11, 1919												
						Aug. 18, 1919	7			x	111	463	746.7	.21	117/68	93	.12
						Aug. 23, 1919	12			x	116.8	550	916	.21	127/66	97	.10
						Sept. 1, 1919	21			x	78.1	162	757.3	.17	125/73	90	.13
D.	F	53	Renal calculus in nonfunctioning left kidney	None		June 28, 1919				x	97	352	028.5	.27	207/123	105	.26

rence of symptoms and urine was found to be guinea pig positive for acid-fast bacilli. Despite what was undoubtedly activation of a tuberculous left kidney, there was definite improvement in renal function. The GFR and effective RPF in the remaining left kidney increased from 59.2 and 328 to 87.5 and 402 respectively, the latter two figures being well above those which one would find in any one of two normal kidneys.

Case L. W. W. On June 21, 1949, left nephrectomy was performed for multiple calculi and pyelonephritis. As seen from table 3, GFR in the remaining right kidney had increased from 39.3 to 53.6 while effective RPF had increased from 230 to 267, 68 days following surgery. It should be noted, however, that at the time of the second clearance determination the diastolic blood pressure had reached minimal hypertensive levels. This may have been a factor in the failure of the remaining kidney to show a more uniform increase in function.

Case R. T. M. A 60 year old normotensive white man with a right renal calculus and a normal left kidney was subjected to nephrectomy on December 14, 1948. Renal clearances were determined in the remaining kidney 14, 21 and 56 days postoperatively. Gradual functional hypertrophy is seen to have occurred as evidenced by the progressive increase in GFR and effective RPF. It appears that a greater improvement in function occurs in the 14 to 21 day period than between the 21 and 56 day period in this one case.

Case A. G. A 54 year old normotensive white man with a normal left kidney and an infected right hydronephrosis and hydro-ureter secondary to ureterovesical obstruction by a congenital valve was subjected to right nephro-ureterectomy on August 11, 1949. Renal clearances were determined in the remaining kidney 7, 12, and 21 days postoperatively. As can be seen from table 3, clearances were begun as soon after surgery as his operative condition would permit, namely on the seventh day following surgery. The GFR and effective RPF of 111 and 463 respectively obtained on the seventh day after nephrectomy are normal. It is thought, therefore, that the uninvolved kidney had really begun "taking over function", so to speak, long before nephrectomy in that its functional capacity was at the lower limits of normal for one in his age group. Despite major surgery, therefore, the functional pattern is seen to have shown improvement as manifested by the increase in GFR from 111 to 116.8 and in effective RPF from 463 to 559. We may possibly conclude that compensatory hypertrophy begins as early as the 7th to 12th days following nephrectomy.

Homer Smith, in his Harvard lecture series, described a patient who, during the middle of a clearance period, received bad news. Clearance values immediately dropped and did not return to normal levels until after the period of emotional upset. Very likely, a somewhat different emotional episode was responsible for the marked drop in GFR and effective RPF from 116.8 and 559 to 78.4 and 462 respectively, on the occasion of the third clearance determined 21 days postoperatively. The patient was highly excitable and against the idea of cooperating with the test. The Pm is also seen to have increased, perhaps significantly.

Case L. D. A 53 year old hypertensive white woman was found to have a left renal calculus at the ureteropelvic junction with a resulting nonfunctioning and completely blocked left kidney. At the time of cystoscopy a catheter could not be passed by the stone and urine did not appear at the catheter. The normally functioning right kidney was studied, utilizing bladder urine.

At the age of 28, the diagnosis of a stone in the left kidney was first made. Surgery was never performed and the patient had no further symptoms referable to the stone. At time of admission a large left kidney, which presumably had undergone hydronephrotic atrophy secondary to the stone at the ureteropelvic junction, was found. Compensatory hypertrophy had undoubtedly occurred over the years in that the above values seen in table 3 are definitely within normal limits for one of her age group. In addition, when one considers her degree of hypertension (207/123), and the resulting renal impairment that the hypertension itself produces, then certainly one may say that compensatory hypertrophy has occurred. The hypertension was of 2 years' duration while the calculus disease was of 25 years' duration. It is therefore unlikely that the hypertension was secondary to unilateral kidney disease. Surgery was refused so that further studies were not made.

Methods described have permitted us to follow minute quantitative functional changes in these patients. Certainly the more commonly used pyelograms, blood urea nitrogens, or even phthalein determinations, would not have permitted one to follow such changes in function. One cannot refute these figures which have so definitely demonstrated the actual presence of compensatory functional, if not anatomical, hypertrophy.

Early and remote effects of temporary renal ischemia and infarction on glomerular filtration rate and effective renal plasma flow. In an effort to determine the effects of renal ischemia and infarction upon renal functional patterns, 2 patients, whose protocols are presented, were selected for study.

Smith has stated that "the glomeruli and tubules of normal nephrons may become partly or wholly inactive due to ischemia without losing their potentiality for immediate return of function on the restoration of an adequate blood supply". This has been well illustrated in the following case:

Case L. S. T. A 47 year old white man was subjected to a splenorenal vein shunt for portal hypertension. The left renal pedicle remained clamped for 60 minutes during the time necessary for anastomosis of the splenic and renal veins. Four weeks following surgery, extraction of PAH was determined from the difference between its concentration in both renal veins, obtained by transcardiac renal vein catheterization, and the peripheral blood. It was found that the extraction ratio of the right kidney was 88 per cent, whereas the left, whose pedicle had been clamped for 60 minutes, showed an extraction ratio of only 4.6 per cent. The validity of the extraction figures from the left kidney may be subject to question because of admixture of splenic and renal blood. With insertion of the catheter beyond the anastomotic site, however, only renal vein blood has been obtained.

Seven months postoperatively the patient was again investigated with the idea of noting changes in function over this period. At this time renal clearance patterns were established and are noted in table 4.

No kidney may be traumatized, no matter how little, without deleterious effects. Not always have these effects been measurable. This case illustrates the immediate and remote effects of temporary ischemia. We might normally have dismissed this case after reading a normal pyelogram. The extraction ratio and clearance methods have been utilized to demonstrate very clearly that even in the face of normal pyelograms there is measurable renal damage. One month following the clamping of the left renal pedicle during the splenic-renal vein anastomosis, the left kidney was able to extract only 4.6 per cent of PAH during a single passage, while the right kidney showed a normal extraction ratio of 88 per cent.

It may be seen from table 4 that a definite difference in the clearance patterns of the 2 kidneys was observed even though it was thought that sufficient time had elapsed for the left kidney to "come back", so to speak. The glomerular filtration rate of the left kidney was 38 as compared with 52 in the right. Effective renal plasma flow in the left kidney was 174.9 as compared with 280.8 in the right kidney.

It has been extremely interesting to follow functional patterns, along with the correlated clinical course, in a patient considered to have what we might term a "Goldblatt half" of a horseshoe kidney.

Case J. S. G. A 35 year old white man was found to have a 2 cm. by 3 cm. calculus in the left half of a horseshoe kidney. On January 3, 1947, a left pyelolithotomy was performed at which time an aberrant artery supplying the upper one-third of the left kidney was accidentally cut and subsequently ligated. There was almost immediate discoloration of the upper third of the kidney supplied by the involved aberrant vessel. The stone was removed but the infarcted portion of the kidney was not resected.

Preoperatively the patient had a normal blood pressure of 124 systolic and 75 diastolic. The blood pressure and renal clearance patterns were followed in this patient for 2 years postoperatively and are seen in table 4.

By April 1947, three months postoperatively, the patient developed hypertension (185/122). Renal infarction as the etiology of his hypertension was suggested. On June 10, 1947, a left heminephrectomy for renal infarction and symptomatic hypertension was performed. The removed specimen revealed infarction of a major portion of the kidney.

In table 4 is seen the preoperative clearance patterns in this patient before nephrectomy was performed. At that time (April 26, 1947) GFR was seen to be normal, whereas effective RPF was slightly decreased. Several days later, on May 1, 1947, clearances were repeated at which time individual studies on each kidney were to be determined. Unfortunately, only the ureter of the normal right half of the horseshoe kidney could be catheterized. The effects of peridural block on glomerular filtration rate and effective renal plasma flow were noted at this time and found to be negligible. When a comparison of these two patterns was made, it was seen that the clearances from the right kidney only, with or without peridural metycaine block, were almost similar to the figures in which bladder urine was utilized. This signifies, very likely, that the right or uninfarcted half was doing all the work.

TABLE 4. *Effects of ischemia and infarction upon the glomerular filtration rate and effective renal plasma flow*

DIAGNOSIS	OPERATION	DATE OF OPERATION	DATE OF CLEARANCES	TIME DAYS POST-OPERATIVE	SOURCE OF URINE			GFR	RPF	RBF	AVERAGE			
					Right Kidney	Left Kidney	Bladder	cc per 1.73 sq.m./min.			FF	B.P.	Pm	RR
Portal hypertension and temporary (60 minutes) left renal ischemia	Splenic-renal vein shunt	Oct. 29, 1948												
			May 6, 1949	188	x			52.0	280.8	474.5	.18	110/58	84	.17
						x		38.0	174.9	296.4	.21			.28
Calculus in left half of horseshoe kidney; infarction of segment of left half of horseshoe kidney	Left pyelolithotomy	Jan. 3, 1947										135/74		
			Apr. 26, 1947	113			x	115	562	1060	.20	185/122	153	.14
			May 1, 1947	118	x*			100	591	1119	.16	210/120	165	.14
					†			96	460	868	.21	175/105	140	.16
	Left heminephrectomy	June 10, 1947												
			Jan. 29, 1948	229			x	90	760	1380	.11	144/96	120	.87
			Dec. 6, 1948	545			x	79.9	469	886	.17	173/102	138	.15

nerve block.

Seven months following the left heminephrectomy, clearance patterns were determined again on January 29, 1948. GFR had remained approximately the same as the preoperative figure, whereas effective RPF had increased to 760 which was definitely normal. Blood pressure was seen to have dropped to an almost normal level. With lowering of the blood pressure, therefore, the RPF was seen to have increased to a normal level.

Eighteen months following resection of the infarcted kidney the blood pressure had returned to hypertensive levels and at the same time, GFR and effective RPF had definitely dropped to significantly abnormal levels, 79.7 and 469 respectively.

In the subject whose left renal pedicle was clamped during splenic-renal vein anastomosis, extraction ratios of PAH determined one month postoperatively revealed definite impairment of function in the left kidney. This was to be expected, one might say, so soon after surgery. Seven months later, however, a quantitative difference in function between the two kidneys still existed as manifested by the clearance patterns. This serves again to illustrate the fact that a kidney is composed of microscopic units, the nephrons, and functionally speaking, one should have a scale commensurate with the structure with which one is working. Clearance determinations and extraction ratio methods have served as such a scale. No other kidney function tests in current everyday use would have given us the same information.

The clinical course of the patient subjected to heminephrectomy for renal infarction and hypertension was similar in that pyelograms and urea nitrogen determinations remained normal. When the blood pressure improved following surgery, renal clearance patterns showed commensurate improvement. Eighteen months following surgery, when the blood pressure reached hypertensive levels, clearance patterns also reflected poor renal function. An explanation for the return of blood pressure to hypertensive levels is not within the scope of this work. Whatever factor may be responsible is undoubtedly the same as that which causes elevation of blood pressure following so-called cures of hypertension by nephrectomy for unilateral kidney disease. This case serves well to illustrate what we are slowly learning; namely, that patients subjected to nephrectomy for unilateral kidney disease must be followed for long periods of time before one can speak of cures of hypertension.

Effects of varying types of renal calculus disease upon glomerular filtration rate and effective renal plasma flow. Further investigations were extended to the problem of renal calculus disease and observations were made on three patients with varying types of calculi. Only 1 of the 3 patients could even be considered a borderline hypertensive. The highest blood pressure recorded in this patient (W. F. M.) was 144/96. Although the urines of all 3 patients grew various types of organisms, the infection was not a predominant factor. We may therefore conclude that within limits all changes seen resulted from the calculus disease per se. These patterns are depicted in table 5.

Case G. L. A 40 year old normotensive white man had two small calculi in the left renal pelvis. An excretory urogram showed no evidence of obstruction.

It may be seen in table 6 that the left kidney showed a definite reduction in renal function as manifested both by a decrease in GFR and in effective RPF. Filtration fraction has remained practically the same for both kidneys. Apparently the size of calculi has little relation to the degree of renal impairment that may be expected. With normal blood pressure findings and a uniform decrease in both glomerular filtration rate and renal plasma flow in the diseased kidney, it is possible that reflex vasospasm involving both the efferent and afferent glomerular arterioles might have resulted. Certainly degree of reduction in function is not compatible with the size of calculi. No therapy was instituted in this patient.

Case J. W. S. A 30 year old normotensive white man was found to have four calculi filling the left lower major calyx. Function studies were determined on the individual kidneys preoperatively, and on the left side following left heminephrectomy. The results are seen in table 5.

The bulb catheter could not be passed on the right side postoperatively. Within a period of only 7 weeks following surgery, there was seen to be minimal improvement in the GFR in the operated left kidney, although the renal plasma flow had almost doubled, increasing from 118.5 to 226. This is further evident in the lowered filtration fraction in the left kidney following surgery. Despite removal of one-fourth of functioning kidney parenchyma along with the contained calculi, the renal function improved, especially the effective RPF. Perhaps these factors re-emphasize the possibility of reflex vasospasm secondary to calculi as being one of the dominant factors in the clearance picture. This is especially remarkable when one considers the fact that the lower fourth of the left kidney was resected.

Case W. F. M. A 40 year old white man with borderline hypertension (144/96) had bilateral renal calculi. An excretory urogram revealed a large right renal calculus with no output of dye and a staghorn calculus in a functioning left kidney. Right pyelolithotomy was done first on April 26, 1949, because of the presence of acute symptoms. Seven weeks later, on June 14, 1949, the left staghorn calculus was removed by nephro- and pyelolithotomy. Preoperative and postoperative differential clearances were run on each kidney and are presented in table 5.

By means of renal clearance patterns, this patient has been followed from preoperative abnormal levels through two major surgical procedures to normal postoperative figures. The combined functions of both kidneys preoperatively are well below normal. It is interesting to see that even after right pyelolithotomy there was a decrease in glomerular filtration rate and effective renal plasma flow in the right kidney although the left or unoperated side showed some improvement. Perhaps the right kidney had not had sufficient time for recovery in that the clearances were run only 15 days following surgery. Removal of the obstructing calculus on the right, therefore, was followed by, but did not necessarily cause, improvement in function on the left.

GFR and RPF as presented in table 5 were averages of two to four clearances just as are all clearances presented in this work. It should be noted that glo-

TABLE 5. *Effects of renal calculi upon glomerular filtration rate and effective renal plasma flow*

PATIENT	SEX	AGE	DIAGNOSIS	OPERATION	DATE OF OPERATION	DATE OF CLEARANCES	TIME DAYS POST-OPERATIVE	SOURCE OF URINE			GFR	RPF	RBF	AVERAGE			
								Right Kidney	Left Kidney	Bladder	cc per 1 73 sq m /min.			FF	B.P.	Pm	RR
G. L.	M	40	Left renal calculi	None		Apr. 1, 1949		x			56.6	367	706	.15	118/75	96	.13
									x		25.5	155	298	.16			.32
J. W. S.	M	30	Left lower calyceal calculi			Jan. 3, 1949		x			35.7	184.5	312.7	.19	124/82	103	.33
									x		25.0	118.5	200.8	.21			.51
				Left heminephrectomy	Dec. 16, 1948												
						Feb. 7, 1949	53		x		29.7	226	389.6	.13	120/88	104	.26
W. F. M.	M	40	Large right renal calculus, left staghorn calculus			Apr. 21, 1949		x			40.6	241	415.5	.16	142/93	117	.27
									x		40.1	191	329.3	.13			.35
				Right pyelolithotomy	Apr. 26, 1949												
						May 11, 1949	15	x			38.9	162.5	285	.17	144/90	117	.41
									x		59.5	276.8	485.6	.21			.24
				Left pyelolithotomy	June 14, 1949												
						June 27, 1949	13			x	117	559	1016.3	.21	135/90	113	.11
						Sept. 9, 1949	136			x	164	719	1438	.22	136/75	105	.07

merular filtration rates in both periods were consistent with each other, while effective renal plasma flow showed a definite decrease from the first clearance of 220.9 on the right and 394.5 on the left, to 104.2 on the right and 159.1 on the left. This change would be compatible with a decrease in the extraction ratio of PAH following ureteral stimulation by the indwelling catheters. This factor should be considered not only in this case but in all in whom ureteral catheters are utilized.

After an analysis of the clearance patterns in these patients is made it is apparent that the size of renal calculi is not directly proportional to degree of malfunction. Small stones, the ones we tend to leave unoperated, or agree to "watch", also show their mark as manifested by measurable changes in GFR and effective RPF.

It has once again been shown that current functional studies in everyday use will not permit us to draw final conclusions concerning the true status of the kidney. These patients had normal blood urea nitrogens and essentially normal pyelograms. Yet, the more refined quantitative methods used in this study have shown measurable changes in function following varying types of surgery.

Studies of glomerular filtration rate and effective renal plasma flow in miscellaneous surgical kidney diseases. In addition to the establishment of renal clearance patterns in the aforementioned disease entities, several other types of kidney disorders often encountered by the urologist were studied. The findings are summarized in table 6.

Case H. J. K. A 25 year old white man with hypospadias and a horseshoe kidney had normal clearances as could be expected.

Case F. C. P. A 62 year old white man had a clear cell carcinoma (hypernephroma) which involved the right kidney. Function of the tumor-containing right kidney was dependent upon the degree of replacement of functioning parenchyma by nonfunctioning tumor. This was verified when it was found that the tumor mass occupied and replaced about 75 per cent to 80 per cent of the right kidney parenchyma. As can be seen in table 6, the GFR and effective RPF of the left kidney were almost five times greater than that of the right tumor-containing kidney. Postoperative studies of the remaining left kidney were not made.

Case M. H. A 56 year old white man with polycystic kidneys had been followed for 2 years. Although the blood urea nitrogen ranged between 41 mg. per cent and 99 mg. per cent, the patient remained asymptomatic. Renal clearances were so poor in this patient that tabulation was not deemed justified. The calculated glomerular filtration rate and renal plasma flow for each kidney was approximately 1.75 and 3.8 respectively. These figures are meaningless when we try to utilize them as actual measurements of the glomerular filtration rate and renal plasma flow. They serve only as a rough index concerning the severity of the disease process. Levels of PAH were so low in the urine that examination was made for the acetylated form of PAH with the thought that perhaps the kidneys were acetylating the PAH. This proved not to be the case since none was found. At levels as described this test is certainly not a valid measure of renal blood flow.

TABLE 5. *Effects of renal calculi upon glomerular filtration rate and effective renal plasma flow*

PATIENT	SEX	AGE	DIAGNOSIS	OPERATION	DATE OF OPERATION	DATE OF CLEARANCES	TIME DAYS POST-OPERATIVE	SOURCE OF URINE			GFR	RPF	RBF	AVERAGE			
								Right Kidney	Left Kidney	Bladder	cc per 1.73 sq.m./min.			FF	B.P.	Pm	RR
. L.	M	40	Left renal calculi	None		Apr. 1, 1949		x			56.6	367	706	.15	118/75	96	.13
									x		25.5	155	298	.16			.32
. W. S.	M	30	Left lower calyceal calculi			Jan. 3, 1949		x			35.7	184.5	312.7	.19	124/82	103	.33
									x		25.0	118.5	200.8	.21			.51
				Left heminephrectomy	Dec. 16, 1948												
						Feb. 7, 1949	53		x		29.7	226	389.6	.13	120/88	104	.26
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									x		40.1	191	329.3	.13			.35
				Right pyelolithotomy	Apr. 26, 1949												
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									x		59.5	276.8	485.6	.21			.24
				Left pyelolithotomy	June 14, 1949												
						June 27, 1949	13			x	117	559	1016.3	.21	135/90	113	.11
						Sept. 9, 1949	136			x	164	719	1438	.22	136/75	105	.07

merular filtration rates in both periods were consistent with each other, while effective renal plasma flow showed a definite decrease from the first clearance of 220.9 on the right and 394.5 on the left, to 104.2 on the right and 159.1 on the left. This change would be compatible with a decrease in the extraction ratio of PAH following ureteral stimulation by the indwelling catheters. This factor should be considered not only in this case but in all in whom ureteral catheters are utilized.

After an analysis of the clearance patterns in these patients is made it is apparent that the size of renal calculi is not directly proportional to degree of malfunction. Small stones, the ones we tend to leave unoperated, or agree to "watch", also show their mark as manifested by measurable changes in GFR and effective RPF.

It has once again been shown that current functional studies in everyday use will not permit us to draw final conclusions concerning the true status of the kidney. These patients had normal blood urea nitrogens and essentially normal pyelograms. Yet, the more refined quantitative methods used in this study have shown measurable changes in function following varying types of surgery.

Studies of glomerular filtration rate and effective renal plasma flow in miscellaneous surgical kidney diseases. In addition to the establishment of renal clearance patterns in the aforementioned disease entities, several other types of kidney disorders often encountered by the urologist were studied. The findings are summarized in table 6.

Case H. J. K. A 25 year old white man with hypospadias and a horseshoe kidney had normal clearances as could be expected.

Case F. C. P. A 62 year old white man had a clear cell carcinoma (hypernephroma) which involved the right kidney. Function of the tumor-containing right kidney was dependent upon the degree of replacement of functioning parenchyma by nonfunctioning tumor. This was verified when it was found that the tumor mass occupied and replaced about 75 per cent to 80 per cent of the right kidney parenchyma. As can be seen in table 6, the GFR and effective RPF of the left kidney were almost five times greater than that of the right tumor-containing kidney. Postoperative studies of the remaining left kidney were not made.

Case M. H. A 56 year old white man with polycystic kidneys had been followed for 2 years. Although the blood urea nitrogen ranged between 41 mg. per cent and 99 mg. per cent, the patient remained asymptomatic. Renal clearances were so poor in this patient that tabulation was not deemed justified. The calculated glomerular filtration rate and renal plasma flow for each kidney was approximately 1.75 and 3.8 respectively. These figures are meaningless when we try to utilize them as actual measurements of the glomerular filtration rate and renal plasma flow. They serve only as a rough index concerning the severity of the disease process. Levels of PAH were so low in the urine that examination was made for the acetylated form of PAH with the thought that perhaps the kidneys were acetylating the PAH. This proved not to be the case since none was found. At levels as described this test is certainly not a valid measure of renal blood flow.

TABLE 6. *Renal clearance patterns in miscellaneous surgical kidney diseases*

PATIENT	SEX	AGE	DIAGNOSIS	OPERATION	DATE OF OPERATION	DATE OF CLEARANCE	TIME DAYS POST-OPERATIVE	SOURCE OF URINE			GFR	RPF	RBF	AVERAGE			
								Right Kidney	Left Kidney	Bladder	cc per 1.73 sq.m./min.			FF	B.P.	Pm	RR
H. J. K.	M	25	Horseshoe kidney	None		Jan. 25, 1949		x			50	324	535.3	.15	140/90	115	.18
									x		51	343	672.5	.15			.17
F. C. P.	M	62	Right renal carcinoma, (hypernephroma)			Dec. 6, 1948		x			19.7	93.1	169.3	.21	137/92	115	.68
									x		48.3	182.7	332.2	.26			.34
				Right nephrectomy	Jan. 25, 1949												
R. B. P.	M	48	Right pyelonephritis			Nov. 28, 1949			x			91.8			165/115	140	
				Right nephrectomy	Nov. 29, 1949												
D. E. F.	M	66	Benign prostatic hypertrophy			Apr. 7, 1948				x	36.2	259	440	.14	120/60	90	.09
				Perineal Prostatectomy	Apr. 14, 1948												
						Apr. 28, 1948	14			x	94	568	847	.16	110/50	80	.20

Case R. B. P. A 48 year old white man was found to have a chronic atrophic pyelonephritis which was secondary to removal of stones from the right kidney 3 years previously. The blood pressure at the time of admission was 200 systolic and 120 diastolic as recorded by the admitting officer. Later examination by the intern revealed blood pressure readings of 130 systolic and 90 diastolic. As can be seen from table 6 effective RPF of the left kidney was definitely lower than normal. Because of definite marked stricture formation in the ureter of the right pyelonephritic kidney, clearances could not be run on this side. Extraction ratios were therefore determined in both kidneys on the day before operation. At that time the right kidney was able to extract 7.1 per cent and 5.9 per cent of PAH while the so-called normal left kidney showed extraction ratios of PAH varying between 88.5 per cent and 91.6 per cent, the latter figure being well within normal limits.

Following nephrectomy the patient's blood pressure dropped to definitely normal levels. He had been followed for 7 weeks at which time his blood pressure ranged between 120 to 130 systolic and 60 to 70 diastolic. This patient should be followed for a long period before evaluating him as a possible cure for hypertension.

Case D. E. F. A 66 year old normotensive white man was subjected to perineal prostatectomy for benign prostatic hypertrophy. The figures seen in table 6 following surgery are definitely within normal limits for a man of his age group. There is a definite increase both in glomerular filtration rate and in renal plasma flow following prostatectomy. It is important to note that the level of the blood urea nitrogen was the same before and after prostatectomy so that this figure which is usually used as a basis for proceeding with surgery certainly does not reflect degree of improvement, nor can it be taken as a quantitative measurement of improvement in renal function in this case. This is especially evident when we see that the glomerular filtration rate had almost tripled and the renal plasma flow had easily doubled following prostatectomy.

Effects of urethral dilatation and bladder neck resection on extraction ratio, glomerular filtration rate and effective renal plasma flow in the dog. It may be seen in table 7 that neither dilatation of the urethra and bladder neck, nor actual resection of the bladder neck in one dog, resulted in any significant changes in the renal clearance patterns.

In the first dog, GFR and effective RPF actually increased from 24.8 and 49.8 respectively to 27.1 and 55.3 after urethral dilatation, and to 29.7 and 54.7 respectively after bladder neck resection. The same slight increase occurred in the second dog.

In the third dog dilatation of the urethra produced a significant reduction in the extraction ratio of PAH from 69.7 to 48.3, while in the fourth dog, the extraction of PAH after dilatation of the urethra increased from 59 to 64.9.

Insufficient evidence is at hand to draw many conclusions. It appears, however, that urethral dilatation and "prostatectomy" in these dogs did not alter the clearance patterns or the extraction ratio. In only one dog did the kidneys show a significant drop in the extraction ratio. Still one wonders what changes occur in the kidneys of patients subjected to transurethral prostatectomy or to

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								Right Kidney	Left Kidney	Bladder	cc per 1 73 sq m /min			I I	B P	Pm	RR
H J K	M	25	Horseshoe kidney	None		Jun 25, 1949		✓	✓		50 54	324 343	535 3 672 5	15 15	140/90	115	18 17
F C P	M	62	Right renal carcinoma (hypernephroma)			Dec 6, 1948		✓	✓		19 7 48 3	93 1 182 7	169 3 332 2	21 26	137/92	115	68 34
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TABLE 7. *Results of urethral and bladder neck dilatation and bladder neck resection upon renal clearance pattern and extraction ratio in the dog*

DOG NO	WEIGHT	OPERATION	RIGHT KIDNEY	LEFT KIDNEY	GFR	RPF	RBF	FF	PER CENT PAH EXTRACTED
					cc per 1.73 sq m /min				
1	25 lbs.		x		23.9	46.6	84.7	.51	
			x		30.8	39.4	71.6	.53	
			x		29.7	63.4	115.2	.46	
					Average 28.1	49.8	90.5	.50	
		Dilatation of urethra	x		27.1	55.3	100.5	.48	
		Resection of bladder neck	x		29.7	54.7	99.4	.54	
2*	23 lbs.		x		7.1	10.4	17.3	.68	
			x		6.0	10.6	17.6	.56	
					Average 6.5	10.5	17.45	.62	
		Resection of bladder neck	x		9.5	17.0	28.3	.55	
3	21 lbs.								71.1
									68.4
									Average 69.7
		Dilatation of urethra							48.3
4	18 lbs.								59.7
									58.4
									Average 59.0
		Dilatation of urethra							64.9

* Clearances in this dog were determined on a falling blood level of both PAH and THIO. There was a fairly good agreement between the periods, however, so that some conclusions may still be drawn.

simple urethral dilatation during the actual operative procedures. Some factor produces anuria in a few of these patients.

DISCUSSION

Compensatory hypertrophy. The position of the urologist who must evaluate a patient for renal surgery is in many instances not an enviable one. Not only must the diseased side be studied but the status of the so-called healthy kidney is to be taken into account. That a remaining kidney does "take over" there can be no doubt. When, however, we are compelled to speak in terms of degrees of "taking over" we have heretofore dealt mostly in the realm of theory and abstraction with very little quantitative evidence to back up our beliefs. The term "compensatory hypertrophy" has been loosely used to designate improvement in the function of a kidney once its mate is removed. With the advent of more refined methods of measuring renal reserve, actual physiological hypertrophy in terms of improvement in GFR and RPF may now be calculated.

Rowntree's initial studies with PSP included investigative work with Young's urological patients. In several cases, studied at intervals of a few days following nephrectomy, the function ranged closely to that which existed in the kidney before surgery. At 3 to 4 weeks following nephrectomy, function of the remaining kidney was found not only to equal the combined preoperative function of both the normal and abnormal kidneys, but to have surpassed it. Approximately 3 weeks was given for this compensatory hypertrophy to have occurred.

In 1924 Addis, Myers, and Oliver performed unilateral nephrectomies in rabbits. Within 15 to 33 days after surgery the average clearances were 63 per cent of preoperative values. By 4 months the clearances were 79 per cent of the preoperative levels and the remaining kidney was observed to undergo actual anatomical hypertrophy. Rhoads, Alving, Hiller, and Van Slyke in 1934, showed that after nephrectomy in animals the weight of the residual kidney increased by 3 per cent to 27 per cent. The urea clearance following unilateral nephrectomy was also found to have reached normal levels after 6 months. These workers concluded that in man, too, the urea clearance would eventually reach normal levels after removal of a kidney. This work of these two groups of investigators permits us to speak of actual hypertrophy following nephrectomy. They have shown that improvement in urea clearance means a true increase in kidney mass.

In a very meticulous study of 5 hypertensive patients with unilateral kidney disease in whom nephrectomy had failed insofar as cure of hypertension was concerned, Friedman, et al. made interesting observations to the effect that in all 5 patients, diodrast and inulin clearances in the remaining kidney improved following nephrectomy.

The term "renal counterbalance" has been applied by Hinman (quoted from Berglund) to the functional reserve of the remaining kidney following nephrectomy. The relative renal insufficiency during the first few days following nephrectomy was not considered proportional to the amount of renal mass removed. It was his belief that this renal insufficiency was compensated for by a true anatomical hypertrophy. A mass hypertrophy of the kidney as distinguished from "circumscribed" hypertrophy, is that type which follows removal of its mate. Hinman further stated that functional compensation occurs before actual anatomical hypertrophy which requires 30 to 40 days. It was Hinman's conclusion that the "application of the theory of renal counterbalance is handicapped by the limitations in the methods of clinical study. There is no way of testing renal reserve. Functional tests are empirical. None of them tell all that a kidney is capable of doing." This is no longer true in that we are now able to measure renal reserve, and functional tests are no longer so empirical.

Renal ischemia and infarction. The increasing frequency with which conservative renal surgery, in lieu of sacrifice of the kidney, is performed has placed certain demands upon our knowledge of renal function. Nephrolithotomy, pyelolithotomy, and heminephrectomy for calculus disease are but a few of the examples of conservative surgery. Nephrolithotomy for staghorn calculus, heminephrectomy for lower calyceal stones and for disease in one-half of a horseshoe kidney, symphysiotomy in the horseshoe kidney, and similar procedures are all formidable operations. The need for conservative treatment in the horseshoe kidney and in the patient with only one kidney need only be mentioned.

These, and many other major surgical procedures have been made possible not only by the increasing skill and technical knowledge of the operator, but also by means of adequate control of the renal pedicle vessels during the time of surgery. As is the case with the use of the tourniquet in the extremities, the time factor is an all-important one. Many urologists know within their own minds the upper limits of normal that pedicle clamps may be left in place. Some men have even gone so far as to quote exact figures concerning the length of time that clamps may be left in place. Yet there has been little study concerning the actual measurable damage in these kidneys with temporary renal ischemia. That the kidney is damaged there can be no doubt. The quantitative degree of impairment, however, and the long term effects have been too poorly studied.

The renal clearance methods utilized as measurements of renal function have been used in a study of this problem. These methods combined with the use of the renal extraction ratio of PAH have been utilized to good advantage and have made possible a quantitative measurement of the immediate and remote effects of temporary ischemia in one case and of renal infarction in another.

Whereas arterial blood may be obtained without difficulty from a peripheral vessel, the problem has been to collect renal vein blood in this determination of the extracting power of the kidney. In animals, the problem is answered by simple exteriorization of the kidney with withdrawal of renal vein blood at the discretion of the investigator. In the human this problem has been solved by the technique of catheterization of the renal vein by passage through the right heart.

Hamilton, Phillips, and Hiller have studied the effect of renal ischemia in the dog. It was their conclusion that dogs uniformly survived clamping of the renal artery for 2 hours. Some dogs lived after the clamp had been in place for 3 or

4 hours, but all died in uremia when the clamp was left for a longer period of time.

Extraction ratios and renal plasma flow were then measured in these animals whose arteries were clamped for periods of 20 to 120 minutes. It was found that extraction ratios of PAH and creatinine were not seriously affected after 20 minutes of clamping. With 2-hour ischemia the extraction ratios were between 9 per cent and 63 per cent of pre-ischemic levels.

Scheibe, Giraldi, and Vermeulen have performed unilateral nephrectomy in dogs and in rats and have subsequently studied the effects of 15, 60, 90, 105, and 150 minutes clamping of the remaining renal vein and of the entire renal pedicle. They concluded that the renal vein may be occluded for 30 minutes whereas the entire pedicle may be clamped for 90 minutes in the rat. These figures were doubled in the dog. Their results were somewhat similar to those of Hamilton and his co-workers. The mortality rates were found to be increased proportionately with the length of time the pedicle clamps were left in place.

A discussion of the role of unilateral kidney disease in the etiology of hypertension is not within the scope of this paper. Since the original description of the "Goldblatt kidney," reports in the literature of cure of hypertension following removal of a single diseased kidney have been numerous. Many writers have established definite criteria for acceptance of such cases as true cures. With more critical standards of evaluation and with observation over longer periods of time, many of the cases at first considered cured of hypertension by nephrectomy for unilateral disease have been found to have shown return of blood pressure to hypertensive levels.

Friedman, Jarman, and Klemperer have produced hypertension in rats by wrapping cellophane around a single kidney, thereby resulting in perinephritis. Nephrectomy subsequently lowered the blood pressure but not to normal levels. It was felt that irreversible changes had occurred in the remaining kidney which were responsible for the persistence of an elevated blood pressure. This may have occurred in the case presented (J. S. G.) and in many similar cases which were improved but not cured following nephrectomy.

Calculus disease. The ill effects of renal calculus disease are dependent upon degree of infection and obstruction, either of which, if severe enough, is capable of producing renal insufficiency. The functional patterns in kidneys with stones are dependent upon many factors. A strategically placed calculus, no matter how small, at the ureteropelvic junction may interfere with adequate urine flow so as to make urine collections impossible and the clearance studies of no value. Larger stones may produce less damage than small ones unless they are of sufficient size to obstruct all papillae; for example, staghorn calculi. Associated infection in the form of pyelonephritis may alter the renal function. Co-existent hypertension, whether primary or whether secondary to calculus pyelonephritis, undoubtedly affects the clearance patterns.

Prostatic obstruction. Proper preoperative evaluation and preparation of the elderly patient for prostatectomy are essential and are considered by many as being as important as the operative procedure itself. No longer do we bring patients in acute urinary retention from the streets to the operating room. Even the proponents of transurethral surgery learned by bitter experience in the early thirties that this method, as well as other methods of approach to the prostate, required a well-prepared patient. Long before this time, however, urologists were aware of the fact that catheter drainage with reduction of the urea nitrogen to low stable levels was an essential prerequisite to the well-being of the patient.

The purpose of prostatectomy is to continue what catheter drainage has started: namely, to improve renal function. That this purpose has been definitely accomplished is seen in the data in table 6 (case D. E. F.). In this type of study it is especially important to select a patient with normal blood pressure findings so that the values obtained either preoperatively or postoperatively could not be attributed to the hypertensive disease itself.

Reflex anuria. It has been long known, and yet poorly understood, that oliguria and even anuria have followed such urologic procedures as transurethral surgery, cystoscopy, or even mere passage of sounds.

The exact causative mechanism for these and similar cases is not known. Kasten has classified anuria into four groups of which one, the "circulatory or prerenal," includes such cases. This group includes the cases of anuria which are secondary to peripheral irritation:

1) "Urethrorenal" reflex, the type of anuria seen following passage of catheter or sounds, or more commonly found secondary to transurethral prostatectomy.

2) "Ureterorenal" reflex, secondary to passage of ureteral catheters or rough handling of ureters at surgery. Kapsammer as early as 1907 noted a decrease in renal function following introduction of ureteral catheters. Whereas he described anuria following ureteral catheterization, it is interesting to note that in some cases polyuria followed.

3) "Vesicorenal" reflex: Pflaumer in 1919 observed an inhibition of renal function as the bladder pressure was increased. Kasten has reported a case of anuria secondary to a simple suprapubic prostatectomy. For empirical and not for scientific reasons the dictum never to quickly decompress the bladder of a patient in acute urinary retention is followed. Perhaps some vesicorenal reflex is initiated which may be followed by deleterious effects.

Many additional factors must be considered in this matter of reflex anuria which is primarily a urological problem. Various contributing factors have been listed. These include:

1) Severe painful stimuli are likely to produce falls in blood pressure. Wolfe described a definite decrease in diodrast and inulin clearances and in urine flow following application of a painful stimulus to the head. He has reported a fatal case of anuria which followed a painful cystoscopy and has suggested that a reflex reduction in renal blood flow may be the initiating factor progressing to oliguria or even to anuria. Similar cases of anuria secondary to transurethral prostatectomy are unfortunately too numerous to mention.

2) Those cases of transurethral prostatectomy which may succumb may be due to simple blood loss and shock. It is known that the blood pressure must

reach certain levels to maintain glomerular filtration. Whether the drop in blood pressure is secondary to blood loss or to spinal anesthesia, as suggested by some, is not too important. The significant factor is the fall below levels necessary to maintain filtration. In those cases of shock secondary to blood loss a decrease in cardiac output is noted. Yet Maluf has found that the renal blood flow does not remain a fraction of the cardiac output but that instead it drops even more than does the cardiac output.

Selkurt has found the plasma extraction of PAH to be maintained at normal levels in dogs as long as the systolic blood pressure remains above 60 to 80 mm. of mercury pressure. The diodrast extraction has been found to fall below normal levels whenever systolic blood pressure reaches figures below the aforementioned. It may be stated, therefore, that in dogs in which severe bleeding has been encountered to degrees sufficient to produce a drop in blood pressure to 60 mm. of mercury, there is a rise in renal vascular resistance and a subsequent drop in renal blood flow. With subsequent increase in severity of the hypotension, anuria ensues. Blood loss, therefore, may have been one of the factors which accounted for the low clearance and extraction figures obtained in one of the dogs utilized in this work.

3) The anuria which follows crushing injuries is thought to be secondary to the presence of substances produced by the damaged tissues. This type of anuria was seen in the crushing injuries which followed the air raids in London.

4) Hemoglobinemia and intravascular hemolysis following transurethral prostatectomy, in which distilled water is used for the irrigating fluid, have been suggested as playing a role in the production of anuria. These cases, as well as those in the preceding group, may be classified together as being a small part of the group of lower nephron nephroses.

5) Homer Smith, in a discussion at the 1940 meeting of the American Physiological Society, discussed the role of anesthesia insofar as it affected renal function. He has described abnormally low extraction ratios in humans under various anesthetics. This is a factor of some importance in that the dogs employed in this experiment were under fairly deep anesthesia. This, too, may account for the low extraction ratios obtained.

6) By injection lysed erythrocytes, Maluf has produced a renal shutdown in dogs. This may be comparable to the situation in transurethral prostatectomy which is followed by anuria. Maluf found no shunting of blood from the cortex to medulla as did Trueta. The latter has, in fact, described anuria with zero clearances in dogs, in whom appreciable amounts of blood were flowing through the kidney. This has been attributed to diversion of the intrarenal blood flow from the cortex to the medullary pathway. Trueta has gone so far as to conclude that: "The anuria which occurs after various forms of stimuli to the urinary tract, such as the passage of ureteric stone, the rough handling of the ureters during operation or catheterization is undoubtedly due to the operation of the reflex mechanism and it seems more than likely that the effect of this reflex activity is a well-nigh complete diversion of the intrarenal blood flow from cortex to the medullary pathway".

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7) Dehydration, if severe enough, may alter the effective renal blood flow to the extent that the figures obtained are not true measurements. This, too, may have played its role in the dogs used in this experiment, in that no special effort was made to correct dehydration.

That the problem of reflex anuria is a formidable and yet unanswered one is seen by the very existence of the aforementioned theories, none of which are completely satisfactory. It was therefore anticipated that, by the utilization of both the extraction ratio techniques and the clearance methods as described in the preceding section in which human subjects were used. this problem might be better understood by further investigation.

As stated previously, the purpose of this particular work with dogs is merely to introduce a new method of study of this most important problem of reflex anuria. The author realizes that the results are too scanty to draw far-reaching conclusions.

In general, however, it seems that neither dilatation of the urethra and bladder neck nor actual resection of the bladder neck produces significant changes in GFR and effective RPF. Some factors, other than these, must therefore be in operation if we are to explain anuria in which the urethrorenal reflex is even considered as playing a part. That such a reflex is in operation when combined with other factors, such as intravascular hemolysis or drop in blood pressure, is another matter.

SUMMARY AND CONCLUSIONS

The methods described by Homer Smith and his associates permitting simultaneous measurements of glomerular filtration rate and effective renal plasma flow have been utilized in this clinical and experimental study in which 107 clearances have been determined in 16 human subjects and in 4 dogs. These clearances have been tabulated as renal clearance patterns consisting of determinations, direct and calculated, of glomerular filtration rate, effective renal plasma flow, renal blood flow, filtration fraction, and crude renal resistance. Observations have been made in a wide variety of urological disease entities including the most commonly seen "surgical kidneys". Based upon these clearance patterns the following conclusions have been drawn:

1) Compensatory hypertrophy of one kidney following removal or cessation of function of its mate, is a unique physiological process which may actually be measured in quantitative terms.

2) Beginning functional hypertrophy has been found as early as the seventh to twelfth day following nephrectomy. That the process is a continuous one is manifest by improvement in function over periods of several months. In the one patient studied 14, 21, and 56 days following nephrectomy, a greater degree of improvement in function was found to have occurred in the 14 to 21 day period than in the 21 to 56 day period. In the patient whose left kidney had been slowly destroyed over a period of many years by an obstructing stone at the ureteropelvic junction, the function of the right kidney was found to be equal to that

of two normal kidneys, despite the fact that the patient had severe hypertension.

3) Temporary periods of emotional upset may cause measurable and significant diminution in function.

4) Degree of compensatory hypertrophy is of course dependent to some extent upon the normalcy of the remaining kidney. Activation of a previously quiescent remaining tuberculous kidney may prevent full return to function although in one case there was still some improvement.

5) Clearance patterns established in cases of renal ischemia and infarction reveal a uniform decrease in function.

6) In a patient whose left renal pedicle remained clamped for 60 minutes during which time a splenic-renal vein anastomosis for portal hypertension was performed, marked difference in the extraction ratios of the two kidneys was demonstrated. Despite persistently normal pyelograms and urea nitrogen determinations, clearance patterns 7 months following surgery revealed definitely poor function in the left kidney. Temporary interference with renal blood supply is not, therefore, an innocuous procedure in that functional impairment was seen as late as 7 months following initial surgery.

7) Renal infarction in one-half of a horseshoe kidney resulted in a general decrease in renal function. Following heminephrectomy for infarction and hypertension, renal clearance patterns showed definite improvement with drop in blood pressure. As the blood pressure returned to abnormal levels there was a proportional decrease in renal function. Effective renal plasma flow showed greatest degree of change.

8) Patients with varying types of renal calculus disease show a uniform decrease in function in the involved kidney. Size of calculi is apparently not proportional to degree of malfunction. Following removal of calculi there is improvement in the clearance patterns.

9) In a patient subjected to heminephrectomy for lower calyceal stones there followed improvement in effective renal plasma flow, whereas glomerular filtration rate did not increase. It is postulated that stones may cause a reflex vasospasm with subsequent reduction in effective renal plasma flow.

10) Blood urea nitrogen determinations and other current renal function tests in use for evaluation of patients with benign prostatic hypertrophy do not indicate minute quantitative changes in function which are revealed by clearance patterns. Perineal prostatectomy for benign prostatic hypertrophy resulted in marked improvement in glomerular filtration rate and effective renal plasma flow while the blood urea determination remained at constant levels.

11) Replacement of functioning renal parenchyma by nonfunctioning carcinoma is reflected in the clearance patterns wherein there is a proportional diminution in function in the tumor-containing kidney.

12) Urethral dilatation and "transurethral prostatectomy" in the dog did not result in obvious decrease in renal function. In only one animal did a decrease in the extraction ratio follow urethral dilatation.

13) Introduction of the use of renal clearance patterns into the field of clinical

urology has permitted us to make certain observations which the usual function tests have not. These methods of renal function study call for a revision of current concepts of evaluation of the urological patient.

U. S. Marine Hospital, Norfolk, Va.

REFERENCES

Addis, T., Myers, B. A. and Oliver, J. Regulation of renal activity. Effect of unilateral nephrectomy on function and structure of the remaining kidney. Arch. Int. Med., **34:** 243, 1921.

Berglund, H., et al. The Kidney in Health and Disease. Philadelphia: Lea & Febiger, 1935.

Bradley, S. E., Curry, J. J. and Bradley, G. P. Renal extraction of P-aminohippurate in normal subjects and in essential hypertension and chronic diffuse glomerulonephritis. Fed. Proc., **6:** 79, 1917.

Cabot, Hugh. Modern Urology. Philadelphia: Lea & Febiger, 1936.

Corcoran, A. C., Taylor, R. A. and Page, I. H. Functional patterns in renal disease. Ann. Int. Med., **28:** 560, 1948.

Dukes, C. E. Urine. Examination and clinical interpretation. New York and London: Oxford Univ. Press, 1939.

Friedman, B., Jarman, J. and Klemperer, P. Sustained hypertension following experimental unilateral renal injuries. Effects of nephrectomy. Am. J. Med. Sc., **202:** 20, 1941.

Friedman, M., Selzer, A., Kreutzmann, O. O. and Sampson, J. J. Changes in the blood pressure and in the renal blood flow and glomerular filtration rate of hypertensive patients following unilateral nephrectomy. J. Clin. Invest., **21:** 19, 1942.

Goldblatt, H. Experimental hypertension induced by renal ischemia. The Harvey Lectures, **33:** 237, 1937–38.

Goldring, W. and Chasis, H. Hypertension and hypotensive disease. Oxford: The Commonwealth Fund, 1944.

Goldring, W. and Chasis, H. Sympathectomy and unilateral nephrectomy in the treatment of hypertensive disease. Med. Clin. N. Am., **33:** 751, 1949.

Goldring, W., Chasis, H., Ranges, H. A. and Smith, H. W. Relations of effective renal blood flow and glomerular filtration to tubular excretory mass in normal man. J. Clin. Invest., **19:** 739, 1940.

Hamilton, P. B., Phillips, R. A. and Hiller, A. Duration of renal ischemia required to produce uremia. Am. J. Physiol., **152:** 517, 1918.

Houck, C. R. Statistical analysis of filtration rate and effective renal plasma flow related to weight and surface area in dogs. Am. J. Physiol., **153:** 169, 1918.

Kapsammer, G. Newer methods in diagnosis of kidney disease. Surg., Gynec. & Obst., **4:** 589, 1907.

Karsner, H. T., Hanzal, R. F. and Moore, R. A. Urea clearance after unilateral nephrectomy in dogs. Arch. Path., **17:** 46, 1934.

Kasten, H. E. Etiology of anuria with emphasis on prevention and treatment. Analysis of nine cases. J. Urol., **49:** 93, 1943.

Lamport, H. Formulae for afferent and efferent arteriolar resistance in human kidney. J. Clin. Invest., **20:** 535, 1941.

Maluf, N. S. R. Exteriorization of the canine vesical trigone for experiments on the kidney. Ann. Surg., **130:** 43, 1949.

Newman, E. V., Gilman, A. and Philips, F. S. Renal clearance of thiosulfate in man. Johns Hopk. Hosp. Bull., **79:** 229, 1946.

Phillips, R. A. and Hamilton, P. B. Effect of 20, 60, and 120 minutes of renal ischemia on glomerular and tubular function. Am. J. Physiol., **152:** 523, 1948.

Pitts, R. F. The clearance of creatine in dog and man. Am. J. Physiol., **109:** 532, 1934.

Reubi, F. C. The renal extraction of mannitol and para-aminohippurate compared to their excretions in normotensive and hypertensive subjects. J. Clin. Invest., **27:** 553, 1948.

Rhoads, C. P., Alving, A. S., Hiller, A. and Van Slyke, D. D. The functional effect of explanting one kidney and removing other. Am. J. Physiol., **109:** 329, 1934.

Rowntree, L. G. and Geraghty, J. T. An experimental and clinical study of the functional activity of the kidneys by means of phenolsulphonephthalein. J. Pharm. & Exper. Therap., **1:** 579, 1909–10.

Rowntree, L. G. and Geraghty, J. T. The phthalein test. Arch. Int. Med., **9:** 284, 1912.

Scheibe, J. R., Giraldi, E. and Vermeulen, C. W. The effect of temporary renal vascular occlusion on kidney function. Surgery, **25:** 724, 1949.

Selkurt, E. E.: Comparison of renal clearances with direct renal blood flow under control conditions and following renal ischemia. Am. J. Physiol., **145**: 376, 1946.

Shannon, J. A. and Fisher, S.: The renal tubular reabsorption of glucose in the normal dog. Am. J. Physiol., **122**: 765, 1938.

Shock, N. W.: Kidney function tests in aged males. Geriatrics, **1**: 232, 1946.

Smith, H. W.: The Physiology of the Kidney. London: Oxford Univ. Press, 1937.

Smith, H. W.: Lectures on the kidney. Univ. of Kansas, Lawrence, Kansas. 1943.

Smith, H. W., Goldring, W. and Chasis, H.: The measurement of tubular excretory mass, effective blood flow and filtration rate in the normal human kidney. J. Clin. Invest., **17**: 263, 1938.

Smith, H. W., Finkelstein, N., Aliminosa, L., Crawford, B. and Graber, M.: The renal clearances of substituted hippuric acid derivatives and other aromatic acids in dog and man. J. Clin. Invest., **24**: 388, 1945.

Trueta, J., et al.: Studies of the Renal Circulation. Springfield, Ill.: Charles C. Thomas, 1947.

Warren, J. V., Brannon, E. S. and Merrill, A. J.: A method of obtaining renal venous blood in unanesthetized persons with observations on extraction of oxygen and sodium para-amino hippurate. Science, **100**: 108, 1944.

Wolf, G. A., Jr.: The effect of pain on renal function. A. Research Nerv. & Ment. Dis., Proc., **23**: 358, 1943.

Wolf, G. A., Jr.: Mechanism of reflex anuria. Ann. Int. Med., **23**: 99, 1945.

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U S Marine Hospital, Norfolk, Va

REFERENCES

Addis, T , Myers, B A and Oliver, J Regulation of renal activity Effect of unilateral nephrectomy on function and structure of the remaining kidney Arch Int Med , **34:** 243, 1924

Berglund, H , et al The Kidney in Health and Disease Philadelphia Lea & Febiger, 1935

Bradley, S E , Curry, J J and Bradley, G P Renal extraction of P aminohippurate in normal subjects and in essential hypertension and chronic diffuse glomerulonephritis Fed Proc , **6:** 79, 1947

Cabot, Hugh Modern Urology Philadelphia Lea & Febiger, 1936

Corcoran, A C , Taylor, R A and Page, I H Functional patterns in renal disease Ann Int Med , **28:** 560, 1948

Dukes, C E Urine Examination and clinical interpretation New York and London Oxford Univ Press, 1939

Friedman, B , Jarman, J and Klemperer, P *Sustained hypertension* following experimental unilateral renal injuries Effects of nephrectomy Am J Med Sc , **202:** 20, 1941

Friedman, M , Selzer, A , Kreutzmann, O O and Sampson, J J Changes in the blood pressure and in the renal blood flow and glomerular filtration rate of hypertensive patients following unilateral nephrectomy J Clin Invest , **21:** 19, 1942

Goldblatt, H Experimental hypertension induced by renal ischemia The Harvey Lectures, **33:** 237, 1937–38

Goldring, W and Chasis, H Hypertension and hypotensive disease Oxford The Commonwealth Fund, 1944

Goldring, W and Chasis, H Sympathectomy and unilateral nephrectomy in the treatment of hypertensive disease Med Clin N Am **33:** 751, 1949

Goldring, W , Chasis, H , Ranges, H A and Smith, H W Relations of effective renal blood flow and glomerular filtration to tubular excretory mass in normal man J Clin Invest , **19:** 739, 1940

Hamilton, P B , Phillips, R A and Hiller, A Duration of renal ischemia required to produce uremia Am J Physiol , **152:** 517, 1948

Houck, C R Statistical analysis of filtration rate and effective renal plasma flow related to weight and surface area in dogs Am J Physiol , **153:** 169, 1948

Kapsammer, G Newer methods in diagnosis of kidney disease Surg , Gynec & Obst , **4:** 589, 1907

Karsner, H T , Hanzal, R F and Moore, R A Urea clearance after unilateral nephrectomy in dogs Arch Path , **17:** 46, 1934

Kasten, H E Etiology of anuria with emphasis on prevention and treatment Analysis of nine cases J Urol , **49.** 93, 1943

Lamport, H Formulae for afferent and efferent arteriolar resistance in human kidney J Clin Invest , **20:** 535, 1941

Maluf, N S R Exteriorization of the canine vesical trigone for experiments on the kidney Ann Surg , **130:** 43, 1949

Newman, E V , Gilman, A and Philips, F S Renal clearance of thiosulfate in man Johns Hopk Hosp Bull , **79.** 229, 1946

Phillips, R A and Hamilton, P B Effect of 20, 60, and 120 minutes of renal ischemia on glomerular and tubular function Am J Physiol , **152:** 523, 1948

Pitts, R F The clearance of creatine in dog and man Am J Physiol , **109:** 532, 1934

Reubi, F C The renal extraction of mannitol and para aminohippurate compared to their excretions in normotensive and hypertensive subjects J Clin Invest , **27:** 553, 1948

Rhoads, C P , Alving, A S , Hiller, A and Van Slyke, D D The functional effect of explanting one kidney and removing other Am J Physiol , **109:** 329, 1934

Rowntree, L G and Geraghty, J T An experimental and clinical study of the functional activity of the kidneys by means of phenolsulphonephthalein J Pharm & Exper Therap , **1:** 579, 1909-10

Rowntree, L G and Geraghty, J T The phthalein test Arch Int Med , **9:** 284, 1912

Scheibe, J R , Giraldi, E and Vermeulen, C W The effect of temporary renal vascular occlusion on kidney function Surgery, **25:** 724, 1949

Selkurt, E. E.: Comparison of renal clearances with direct renal blood flow under control conditions and following renal ischemia. Am. J. Physiol., **145:** 376, 1946.

Shannon, J. A. and Fisher, S.: The renal tubular reabsorption of glucose in the normal dog. Am. J. Physiol., **122:** 765, 1938.

Shock, N. W.: Kidney function tests in aged males. Geriatrics, **1:** 232, 1946.

Smith, H. W.: The Physiology of the Kidney. London: Oxford Univ. Press, 1937.

Smith, H. W.: Lectures on the kidney. Univ. of Kansas, Lawrence, Kansas. 1943.

Smith, H. W., Goldring, W. and Chasis, H.: The measurement of tubular excretory mass, effective blood flow and filtration rate in the normal human kidney. J. Clin. Invest., **17:** 263, 1938.

Smith, H. W., Finkelstein, N., Aliminosa, L., Crawford, B. and Graber, M.: The renal clearances of substituted hippuric acid derivatives and other aromatic acids in dog and man. J. Clin. Invest., **24:** 388, 1945.

Trueta, J., et al.: Studies of the Renal Circulation. Springfield, Ill.: Charles C. Thomas, 1947.

Warren, J. V., Brannon, E. S. and Merrill, A. J.: A method of obtaining renal venous blood in unanesthetized persons with observations on extraction of oxygen and sodium para-amino hippurate. Science, **100:** 108, 1944.

Wolf, G. A., Jr.: The effect of pain on renal function. A. Research Nerv. & Ment. Dis., Proc., **23:** 358, 1943.

Wolf, G. A., Jr.: Mechanism of reflex anuria. Ann. Int. Med., **23:** 99, 1945.

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REFERENCES

Addis, T , Myers, B A and Oliver, J Regulation of renal activity Effect of unilateral nephrectomy on function and structure of the remaining kidney Arch Int Med , **34:** 243, 1924

Berglund, H , et al The Kidney in Health and Disease Philadelphia Lea & Febiger, 1935

Bradley, S E , Curry, J J and Bradley, G P Renal extraction of P aminohippurate in normal subjects and in essential hypertension and chronic diffuse glomerulonephritis Fed Proc , **6:** 79, 1947

Cabot, Hugh Modern Urology Philadelphia Lea & Febiger, 1936

Corcoran, A C , Taylor, R A and Page, I H Functional patterns in renal disease Ann Int Med , **28:** 560, 1948

Dukes, C E Urine Examination and clinical interpretation New York and London Oxford Univ Press, 1939

Friedman, B , Jarman, J and Klemperer, P Sustained hypertension following experimental unilateral renal injuries Effects of nephrectomy Am J Med Sc , **202:** 20, 1941

Friedman, M , Selzer, A , Kreutzmann, O O and Sampson, J J Changes in the blood pressure and in the renal blood flow and glomerular filtration rate of hypertensive patients following unilateral nephrectomy J Clin Invest , **21:** 19, 1942

Goldblatt, H Experimental hypertension induced by renal ischemia The Harvey Lectures, **33:** 237, 1937–38

Goldring, W and Chasis, H Hypertension and hypotensive disease Oxford The Commonwealth Fund, 1944

Goldring, W and Chasis, H Sympathectomy and unilateral nephrectomy in the treatment of hypertensive disease Med Clin N Am , **33:** 751, 1949

Goldring, W , Chasis, H , Ranges, H A and Smith, H W Relations of effective renal blood flow and glomerular filtration to tubular excretory mass in normal man J Clin Invest , **19:** 739, 1940

Hamilton, P B , Phillips, R A and Hiller, A Duration of renal ischemia required to produce uremia Am J Physiol , **152:** 517, 1948

Houck, C R Statistical analysis of filtration rate and effective renal plasma flow related to weight and surface area in dogs Am J Physiol , **153:** 169, 1948

Kapsammer, G Newer methods in diagnosis of kidney disease Surg , Gynec & Obst , **4:** 589, 1907

Karsner, H T , Hanzal, R F and Moore, R A Urea clearance after unilateral nephrectomy in dogs Arch Path , **17:** 46, 1934

Kasten, H E Etiology of anuria with emphasis on prevention and treatment Analysis of nine cases J Urol , **49:** 93, 1943

Lamport, H Formulae for afferent and efferent arteriolar resistance in human kidney J Clin Invest , **20:** 535, 1941

Maluf, N S R Exteriorization of the canine vesical trigone for experiments on the kidney Ann Surg , **130:** 43, 1949

Newman, E V , Gilman, A and Philips, F S Renal clearance of thiosulfate in man Johns Hopk Hosp Bull , **79:** 229, 1946

Phillips, R A and Hamilton, P B Effect of 20, 60, and 120 minutes of renal ischemia on glomerular and tubular function Am J Physiol , **152:** 523, 1948

Pitts, R F The clearance of creatine in dog and man Am J Physiol , **109:** 532, 1934

Reubi, F C The renal extraction of mannitol and para aminohippurate compared to their excretions in normotensive and hypertensive subjects J Clin Invest , **27:** 553, 1948

Rhoads, C P , Alving, A S , Hiller, A and Van Slyke, D D The functional effect of explanting one kidney and removing other Am J Physiol , **109:** 329, 1934

Rowntree, L G and Geraghty, J T An experimental and clinical study of the functional activity of the kidneys by means of phenolsulphonephthalein J Pharm & Exper Therap , **1:** 579, 1909–10

Rowntree, L G and Geraghty, J T The phthalein test Arch Int Med , **9:** 284, 1912

Scheibe, J R , Giraldi, E and Vermeulen, C W The effect of temporary renal vascular occlusion on kidney function Surgery, **25:** 724, 1949

SELKURT, E. E.: Comparison of renal clearances with direct renal blood flow under control conditions and following renal ischemia. Am. J. Physiol., **145:** 376, 1946.
SHANNON, J. A. AND FISHER, S.: The renal tubular reabsorption of glucose in the normal dog. Am. J. Physiol., **122:** 765, 1938.
SHOCK, N. W.: Kidney function tests in aged males. Geriatrics, **1:** 232, 1946.
SMITH, H. W.: The Physiology of the Kidney. London: Oxford Univ. Press, 1937.
SMITH, H. W.: Lectures on the kidney. Univ. of Kansas, Lawrence, Kansas. 1943.
SMITH, H. W., GOLDRING, W. AND CHASIS, H.: The measurement of tubular excretory mass, effective blood flow and filtration rate in the normal human kidney. J. Clin. Invest., **17:** 263, 1938.
SMITH, H. W., FINKELSTEIN, N., ALIMINOSA, L., CRAWFORD, B. AND GRABER, M.: The renal clearances of substituted hippuric acid derivatives and other aromatic acids in dog and man. J. Clin. Invest., **24:** 388, 1945.
TRUETA, J., ET AL.: Studies of the Renal Circulation. Springfield, Ill.: Charles C. Thomas, 1947.
WARREN, J. V., BRANNON, E. S. AND MERRILL, A. J.: A method of obtaining renal venous blood in unanesthetized persons with observations on extraction of oxygen and sodium para-amino hippurate. Science, **100:** 108, 1944.
WOLF, G. A., JR.: The effect of pain on renal function. A. Research Nerv. & Ment. Dis., Proc., **23:** 358, 1943.
WOLF, G. A., JR.: Mechanism of reflex anuria. Ann. Int. Med., **23:** 99, 1945.

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REFERENCES

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Berglund, H., et al.: The Kidney in Health and Disease. Philadelphia: Lea & Febiger, 1935.

Bradley, S. E., Curry, J. J. and Bradley, G. P.: Renal extraction of P-aminohippurate in normal subjects and in essential hypertension and chronic diffuse glomerulonephritis. Fed. Proc., **6:** 79, 1947.

Cabot, Hugh: Modern Urology. Philadelphia: Lea & Febiger, 1936.

Corcoran, A. C., Taylor, R. A. and Page, I. H.: Functional patterns in renal disease. Ann. Int. Med., **28:** 560, 1948.

Dukes, C. E.: Urine: Examination and clinical interpretation. New York and London: Oxford Univ. Press, 1939.

Friedman, B., Jarman, J. and Klemperer, P.: Sustained hypertension following experimental unilateral renal injuries. Effects of nephrectomy. Am. J. Med. Sc., **202:** 20, 1941.

Friedman, M., Selzer, A., Kreutzmann, O. O. and Sampson, J. J.: Changes in the blood pressure and in the renal blood flow and glomerular filtration rate of hypertensive patients following unilateral nephrectomy. J. Clin. Invest., **21:** 19, 1942.

Goldblatt, H.: Experimental hypertension induced by renal ischemia. The Harvey Lectures, **33:** 237, 1937–38.

Goldring, W. and Chasis, H.: Hypertension and hypotensive disease. Oxford: The Commonwealth Fund, 1944.

Goldring, W. and Chasis, H.: Sympathectomy and unilateral nephrectomy in the treatment of hypertensive disease. Med. Clin. N. Am., **33:** 751, 1949.

Goldring, W., Chasis, H., Ranges, H. A. and Smith, H. W.: Relations of effective renal blood flow and glomerular filtration to tubular excretory mass in normal man. J. Clin. Invest., **19:** 739, 1940.

Hamilton, P. B., Phillips, R. A. and Hiller, A.: Duration of renal ischemia required to produce uremia. Am. J. Physiol., **152:** 517, 1948.

Houck, C. R.: Statistical analysis of filtration rate and effective renal plasma flow related to weight and surface area in dogs. Am. J. Physiol., **153:** 169, 1948.

Kapsammer, G.: Newer methods in diagnosis of kidney disease. Surg., Gynec. & Obst., **4:** 589, 1907.

Karsner, H. T., Hanzal, R. F. and Moore, R. A.: Urea clearance after unilateral nephrectomy in dogs. Arch. Path., **17:** 46, 1934.

Kasten, H. E.: Etiology of anuria with emphasis on prevention and treatment: Analysis of nine cases. J. Urol., **49:** 93, 1943.

Lamport, H.: Formulae for afferent and efferent arteriolar resistance in human kidney. J. Clin. Invest., **20:** 535, 1941.

Maluf, N. S. R.: Exteriorization of the canine vesical trigone for experiments on the kidney. Ann. Surg., **130:** 43, 1949.

Newman, E. V., Gilman, A. and Philips, F. S.: Renal clearance of thiosulfate in man. Johns Hopk. Hosp. Bull., **79:** 229, 1946.

Phillips, R. A. and Hamilton, P. B.: Effect of 20, 60, and 120 minutes of renal ischemia on glomerular and tubular function. Am. J. Physiol., **152:** 523, 1948.

Pitts, R. F: The clearance of creatine in dog and man. Am. J. Physiol., **109:** 532, 1934.

Reubi, F. C.: The renal extraction of monnital and para-aminohippurate compared to their excretions in normotensive and hypertensive subjects. J. Clin. Invest., **27:** 553, 1948.

Rhoads, C. P., Alving, A. S., Hiller, A. and Van Slyke, D. D.: The functional effect of explanting one kidney and removing other. Am. J. Physiol., **109:** 329, 1934.

Rowntree, L. G. and Geraghty, J. T.: An experimental and clinical study of the functional activity of the kidneys by means of phenolsulphonephthalein. J. Pharm. & Exper. Therap., **1:** 579, 1909–10.

Rowntree, L. G. and Geraghty, J. T.: The phthalein test. Arch. Int. Med., **9:** 284, 1912.

Scheibe, J. R., Giraldi, E. and Vermeulen, C. W.: The effect of temporary renal vascular occlusion on kidney function. Surgery, **25:** 724, 1949.

had pyelograms suggestive of polycystic kidneys, two have died of "kidney trouble" at ages of 35 and 40 years, and two others have been hospitalized elsewhere at the ages of 22 and 39 years because of kidney trouble.

Braasch and Schacht have reported the average age of onset of symptoms at 38.8 years and the average age at death of 50 years with 30 per cent succumbing within two years after the onset of symptoms. Thus, persons so afflicted live into or through their reproductive period of life and the disease is perpetuated according to Mendel's Laws. It is shown in the family cited previously that occurrence may be tragically frequent.

ETIOLOGY

In the literature are many theories of etiology varying from luetic infection to embryological developmental defects. Undoubtedly, it is of embryological origin and the theory of Kampmeier seems to be the most generally accepted. According to this theory, the ureteral bud from the wolffian duct forms the ureter, renal pelvis, major and minor calyces, and the collecting ducts. Mesodermal tissue forms the renal glomeruli and convoluted tubules. Early generations of the two systems connect to form an excretory system. However, the collecting ducts continue to divide and late generations of these ducts connect with the glomerular system while the earlier unineferous tubules undergo successive stages of cystic degeneration. According to Kampmeier: "Every human individual during his fetal life normally passes through a period characterized by the presence of many cystic renal tubules." However, recent work by P. P. Lambert, of the University of Brussels, throws considerable doubt on this theory. Studying serial sections of polycystic kidneys of both infants and adults and making three dimensional graphic reconstructions of individual nephrons, he presents some startling findings. As had been suspected clinically, polycystic disease of the newborn is an entirely different disease from that of the adult. In reconstruction of the cystic nephrons in the infant polycystic kidney, none of the cysts connected with collecting tubules to form a functioning nephron. Similar cysts were found in the adult kidney. These contained glomeruli with patent vessels containing unaltered erythrocytes (suggesting an effective vascular supply was maintained) but no connection with a patent convoluted tubule could be demonstrated. Other cysts were found which appeared as outgrowths along the course of functioning nephrons. In this type, functioning glomeruli and patent tubules which emptied into a papilla were reconstructed.

From these findings, Lambert reasons that, although renal cysts of the adult and newborn are similar in essential structure, the cystic organs differ in topography. Some cysts of the adult and newborn are similarly closed systems; but in the adult cysts occur along the course of the tubules and the renal pelvis. Therefore, he believes the cause and genesis of polycystic disease remain unexplained.

In addition, Lambert studied the physiopathology of adult renal polycystic disease which revealed:

1) The persistence of glomerular activity in the cystic nephrons.

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PRESERVATION OF RENAL FUNCTION IN POLYCYSTIC DISEASE

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Since 1911, at which time Rovsing advocated surgical decompression of polycystic kidneys by multiple puncture of the cysts, most authors have mentioned this procedure only to condemn it. Medical and urological texts advise a close medical regimen in an effort to relieve symptoms and preserve renal function. Likewise, a large group of outstanding urologists advise surgery of any sort only through necessity of relieving intractable pain, uncontrollable hemorrhage, infection, removal of calculi, correction of progressive hydronephrosis due to calculi, pressure of the cysts which are obstructing the ureter, or in suspected complicating tuberculosis or malignancy. A few authors (Bobbitt, Hansman, Rathbun, Reaves, Dodson, Young, Goldstein, and others) have advocated surgical decompression in an effort to halt the progressive destruction of renal tissue by the pressure of gradual distention and enlargement of the cysts.

In the past, the unhappy results of most surgical procedures on polycystic kidneys have probably resulted from uncontrolled infection, which has further embarrassed an already impaired renal function. Since the advent of antibiotics, these urinary tract infections are much more readily controlled. We advocate surgical decompression of polycystic kidneys, in carefully selected cases, in an effort to halt destruction of functioning renal parenchyma by progressive enlargement of the cysts. This is probably best accomplished by: 1) decapsulation; 2) unroofing the larger cysts; 3) puncture of as many of the smaller cysts as possible; 4) application of a sclerosing material to prevent continued secretion of the lining epithelium.

The incidence of polycystic disease in reports of large series of cases is not frequent, but, on the other hand, it is far from a rare disease. At the Mayo Clinic, there were 9 cases in 9,177 necropsies and 193 cases in 680,000 registrations. At the Squier Clinic there were 77 cases in 14,155 admissions. Bell reports a 1:500 occurrence in necropsies while Oppenheimer reports 1 in 356 necropsies and 1 in 3,500 hospital admissions.

The disease shows a definite familial tendency as established by many reports and as well illustrated in one of our patients (L. W.). In this unfortunate family, there were 6 instances of polycystic kidney in 8 siblings with 4 deaths from uremia between the ages of 31 and 43 years. The two surviving individuals showing involvement are now being followed, but as yet show no evidence of renal impairment. The father of that generation and one brother died at the ages of 42 and 43 years with symptoms suggestive of uremia and probably suffered from polycystic disease. In the third generation, one 21-year old male (C. R.), examined by us,

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Read at annual meeting, American Urological Association, Washington, D. C., June 1, 1950.

SELECTION OF CASES FOR SURGICAL DECOMPRESSION

Cahill and Fish reported a series of 58 cases in which operative procedures were performed in 23. They divided those patients requiring operation into the following six groups: 1) where physical trauma to the kidney or spontaneous rupture of cysts caused severe hemorrhage within or around the kidney; 2) renal or perirenal infection; 3) obstruction to the flow of urine caused by pressure of cysts within the kidney or upon the ureter; 4) obstruction or pain due to calculi; 5) tumor or tuberculosis of the kidney; and 6) increasing hypertension without other evidence of renal failure.

Walters and Braasch list the indication for surgery in polycystic kidneys as: A. Primary: 1) pain from distention of cysts; 2) persistent hematuria. B. Secondary: 1) local or diffuse renal infection; 2) renal abscesses; 3) lithiasis; 4) tuberculosis; 5) neoplasm; 6) relief of pressure of cysts to prevent further injury to the remaining renal tissue, as suggested by Rovsing.

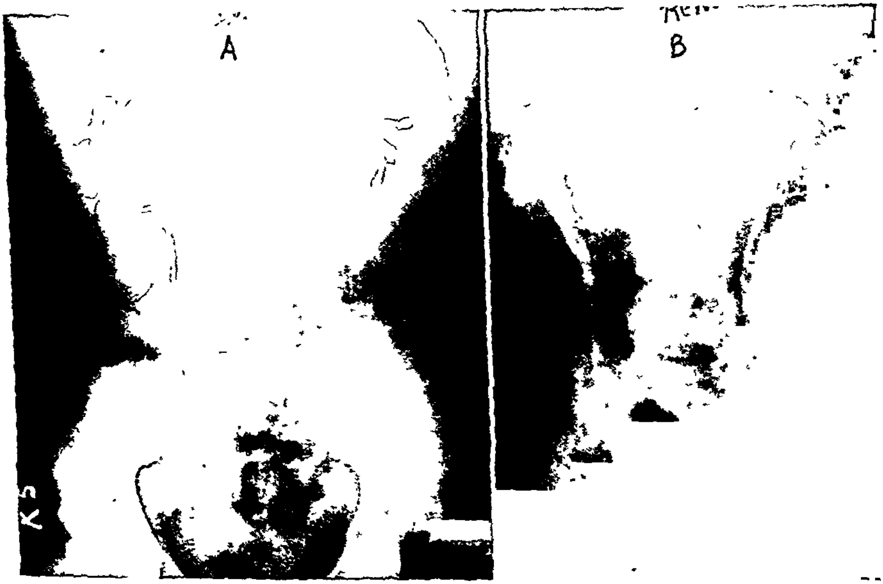

FIG. 1. *A*, excretory pyelogram suggestive of polycystic renal disease. *B*, retrograde pyelogram showing bilateral reduplications.

This discussion will be limited to the last mentioned indication. We believe surgery should not be done in those instances where the patient has no appreciable symptoms, i.e., pain or hematuria, and shows no signs of renal failure. Nor should decompression be advised in persons with evidence of advanced renal failure.

It is believed that decompression should be performed in an effort to preserve renal function in those individuals who are beginning to show some impairment of renal function. This is best evidenced by the more sensitive tests of renal function, i.e., gradual lowering and fixation of specific gravity manifested by urine concentration test and early decrease in urea or inulin clearance. Two persons are

2) The persistence of tubular activity in those nephrons as concerns their ability to reabsorb water, glucose, and urea.

3) The persistence of the ability of the proximal convoluted tubule to store colloidal dyes when these substances are introduced directly into the cystic cavity.

From this, it appears the cystic nephrons of the adult retain their functional activity and play a part in the formation of urine. In fact, in the later stages where atrophy of renal parenchyma is far advanced, the cystic nephrons may be the principal remaining functional elements which are sustaining life.

SIGNS AND SYMPTOMS

The disease may be almost silent, the symptoms causing the individual to seek medical aid being those of a medical nature and pointing to chronic uremic or hypertensive states. The complaints may be of loss of weight, digestive disturbances, dizziness, headaches, malaise, or edema. In some instances, an abdominal mass may have been noted by the person himself with no other difficulty being experienced. More frequently, there will be complaints of pain, or a history of hematuria with or without pain, and recurrent febrile episodes with or without urinary symptoms. The pain may be a dull, chronic, ill defined lumbar ache. In many instances, there are superimposed recurrent attacks of sharp pain, typical of renal colic. It has been theorized that the dull nagging pain may be due to traction on the renal pedicle by the enlarged heavy kidney. The sudden sharp colicky pain may be due to sudden overdistention or rupture of the cysts by hemorrhage into the lumen. If there is gross hematuria with passage of clots, these may cause typical ureteral colic. The hematuria may be recurrent and painless or with colic as noted. In some instances the hemorrhage may be so severe and persistent that surgical measures, even nephrectomy, may be required for its control.

On examination, irregular nodular masses may be palpable in both upper abdominal quadrants. The blood pressure is frequently elevated but may be within normal limits. Urinary findings of pyuria, microscopic or gross hematuria, albuminuria and lowered specific gravity are suggestive of polycystic disease as well as chronic nephritis. Examination of the blood may show anemia, hypoproteinemia, reversal of the A/G ratio, and nitrogenous retention, the latter two usually in more advanced cases.

X-ray findings, by excretory or retrograde pyelograms, typical of polycystic renal disease are essential to a definite diagnosis. Excretory pyelograms are preferable due to the danger of introduction of infection into an extremely susceptible organ or disseminating an already present infection in performing retrograde pyelograms. At times, excretory pyelograms are suggestive but not definitely diagnostic of polycystic disease, and retrograde pyelograms are necessary to establish the diagnosis. Recently, excretory pyelograms seen by us were strongly suggestive of polycystic disease (fig. 1, *A*). However, when retrograde pyelograms were made, the condition proved to be bilateral reduplication of the ureter, pelvis, and kidney (fig. 1, *B*).

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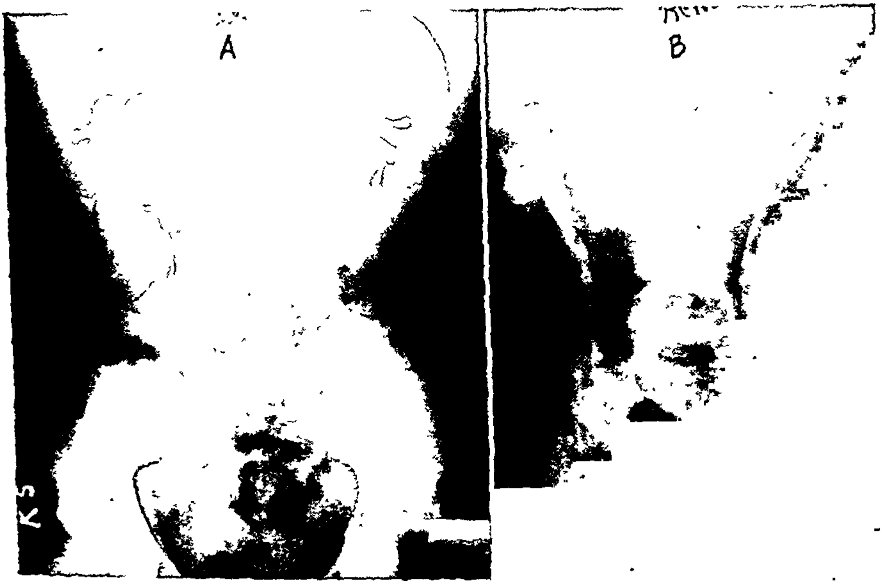

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The capsule is incised along the convex surface of the kidney and stripped from as much of the renal surface as possible, thereby rupturing many of the smaller cysts and probably relieving some intrarenal pressure. The external roof of the larger cysts is excised, at which point other cysts are seen to bulge into the deeper walls of the unroofed cysts. These are likewise opened and evacuated.

The interior of the cystic cavities are then painted with a sclerosing material in an effort to prevent continued secretions or transudation from the lining membrane of the cysts. We have used Zenker's solution for this purpose. Other surgeons have used silver nitrate, sodium morrhuate, or 50 per cent glucose solution. Bleeding must be completely controlled. Hemorrhage from the borders of the excision of the larger cysts can generally be controlled by electrocoagulation, but active bleeding points may require suturing. The generalized oozing from the smaller cysts is best controlled by packing the renal surface with warm saline sheets or oxycel. Multiple Penrose drains are then placed in the evacuated cysts and about the kidney. These remain in place from 10 to 14 days. If there has been sufficient reduction in the size of the kidney, Gerota's fascia is sutured beneath the lower pole to the quadratus lumborum muscle so as to maintain the kidney in position for satisfactory drainage.

Postoperatively penicillin, streptomycin or aureomycin and sometimes sulfonamides are given in high dosages. In our two fatalities the unavailability of streptomycin and aureomycin may have been a deciding factor in their exodus. The fluid intake is maintained above 3000 cc daily. Hemoglobin and blood proteins levels are followed closely and supported with liberal blood transfusions if necessary.

After adequate convalescence, usually three to four weeks, a similar procedure is performed on the opposite side following the same careful preoperative preparation.

CASE REPORTS

Case 1. J. Z., a 42-year old white man, was admitted to McGuire Veterans Administration Hospital April 9, 1949, complaining of right lower quadrant abdominal pain, right flank pain, and nausea without vomiting of 24 hours' duration. The past history was negative except for one attack of right flank pain in 1938. The family history was not contributory. On examination the blood pressure was 150/84; and an irregular, somewhat nodular mass was palpable in the right upper quadrant, extending from the flank to the midline and from the right costal margin downward to the iliac crest. In the left upper quadrant a similar mass could be less distinctly palpated and outlined, but extended from the costal margin down to the umbilicus. The right flank and upper quadrant were tender, the left nontender.

Laboratory studies revealed hemoglobin 13 gm.; white blood cells 10,800 with 84 per cent neutrophils; urinalysis, reaction acid, specific gravity 1.013, albumin and sugar negative; microscopic, an occasional white blood cell and red blood cell; blood proteins 6.2 gm. per cent with albumin 4.1 and globulin 2.1. Excretory pyelograms showed bilateral greatly enlarged renal shadows; there was prompt excretion of contrast medium, but the right calyceal system was compressed, now being followed by us who have no complaints of consequence, but in whom there is definite pyelographic evidence of polycystic disease. Decompression is not being advised at present. However, periodic examinations are being made and when there is the least sign of impairment of renal function bilateral operation will be urged.

PREOPERATIVE PREPARATION

These individuals should be carefully evaluated and every means exhausted to bring them to surgery in the best physical condition and mental attitude possible. On the latter point, we have been impressed that a short time spent in discussing with the patient the disease, reviewing the x-rays and consideration of his future with or without operation, has paid great dividends. The patient is better prepared for surgery and is much more cooperative during a prolonged and sometimes trying postoperative period. The other points routinely stressed in preoperative preparation are:

1) Renal function is improved as much as possible by medical means. This may include a dietary regimen, forcing fluids to the point of proper hydration, and clearing of any existing infection, urinary or otherwise.

2) The cardiac and pulmonary status should be carefully evaluated. Since many of these patients are hypertensives, the advice of the internist and anesthesiologist is of great value.

3) The hemoglobin and total and fractional proteins should be brought to normal levels by transfusions, etc.

4) From 48 to 72 hours before operation antibiotic medication (penicillin and streptomycin or aureomycin) is instituted. In this manner the tissues are well saturated at the time of surgery and any infection encountered in rupturing the cysts should be more readily neutralized.

5) As already mentioned, preoperative retrograde pyelograms should be avoided if possible.

6) Although a debatable point, we decompress the kidney with the better function first.

OPERATIVE PROCEDURE

The choice of anesthesia is quite important. We believe paravertebral block with novocain to be the anesthesia of choice. In many of these individuals the blood pressure is quite elevated and here there is less chance of marked drop in pressure than in spinal anesthesia. Also, the rare danger of toxic action on the renal parenchyma from inhalation anesthesia is avoided.

In placing the patient on the table the kidney rest is not elevated as this may rupture infected cysts of the dependent kidney. Also, elevation of the kidney rest may result in a temporary drop in blood pressure.

After exposure through the usual flank incision, the kidney is handled gently. Thus undue traction on the renal pedicle and trauma to the renal parenchyma is avoided. Next, the kidney is packed off from the renal fossa with warm saline tapes in an effort to prevent contamination from spillage of fluid during evacuation of the cysts.

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Surgical decompression of the left kidney was performed on June 20, 1949, under paravertebral block anesthesia. Postoperative medication was the same and except for a temperature elevation of 101.4 on the first postoperative day, there were no complications. After another uneventful recovery he was discharged July 20, 1949.

On follow-up examination 6 months later he had no complaints, the blood pressure was 150/88, and the kidneys were barely palpable in each upper abdominal quadrant. There was continued improvement in renal function with blood urea nitrogen 18 mg. per cent, urea clearance 56, phenolsulfonphthalein excretion 50 per cent, and Mosenthal concentration to 1.026. The urine was acid with a trace of albumin and microscopically showed a rare red blood cell and 6 to 8 white blood cells per high power field. Culture was sterile. Retrograde pyelograms showed reduction in renal size and improvement in the calyceal structure (fig. 2, *B*).

Case 2. F. W., a 42-year old white man, was admitted to McGuire Veterans Administration Hospital on November 18, 1948, complaining of left flank pain of 3 months' duration. There were no urinary symptoms and the past health had been excellent, the patient doing arduous labor as a truck driver. His father died at the age of 45 of "kidney trouble." On examination the blood pressure was 155/105. A large, irregular mass that moved with respiration was palpable in the left upper quadrant. A questionable mass was present in the right upper quadrant.

Laboratory studies revealed that the blood urea nitrogen was 18 mg. per cent. Urinalysis: specific gravity 1.018 with trace of albumin and 4 to 6 white blood cells microscopically. The phenolsulfonphthalein excretion was 14 per cent in 2 hours with less than 5 per cent in the first half hour. Urea clearance 48 per cent; Mosenthal test showed concentration to 1.020. Blood proteins were 6.3 gm. per cent with albumin 3.9 gm. and globulin 2.4 gm. A plain x-ray showed markedly enlarged renal shadows bilaterally and an excretory urogram showed a calyceal system typical of polycystic kidneys (fig. 3, *A*).

Surgical decompression of the right kidney was performed December 2, 1948, under paravertebral block anesthesia. The kidney was enlarged, being 16 by 14 cm. in size. The surface was covered with cysts ranging from 1 mm. to 3 cm. in diameter. The blood pressure remained stable at 140–150/80–90 during the procedure.

On streptomycin and penicillin intramuscularly and sodium sulfadiazine in the intravenous fluids the postoperative course was uneventful. The drains were removed on the fifteenth postoperative day.

He was discharged from the hospital December 31, 1948, at which time laboratory studies were: Urinalysis: acid reaction; specific gravity 1.017; microscopic 3–4 white blood cells and 10–12 red blood cells and culture negative. Blood urea nitrogen 18 mg. per cent.

He returned March 7, 1949 for decompression of the left kidney. At this time he had no complaints. The blood pressure was 150/100. Laboratory studies: Urine specific gravity 1.013 and 0–2 white blood cells. Blood urea nitrogen 18 mg. per cent. Blood proteins 6.4 gm. per cent with albumin 4.1 gm. and globulin 2.3 gm.

rotated and abnormally low; the left major calyces were elongated and tortuous, suggestive of polycystic renal disease. This was confirmed by retrograde pyelography (fig. 2, *A*)

Renal function studies showed some impairment: urea clearance 35 per cent, phenolsulfonphthalein excretion 20 per cent in 2 hours; Mosenthal concentration 1.010 to 1.014; and blood urea nitrogen 24 mg. per cent.

Surgical decompression of the right kidney was performed April 20, 1949, under paravertebral block anesthesia. The kidney was greatly enlarged, measuring 20 by 10 by 8 cm. with a large cyst 6 cm. in diameter at the lower pole, while the entire surface was studded with smaller cysts. The blood pressure remained stable at 140/80 throughout the procedure and on termination the kidney was much reduced in size. With penicillin and streptomycin intramuscularly and sodium sulfadiazine in intravenous fluids, the postoperative course was smooth.

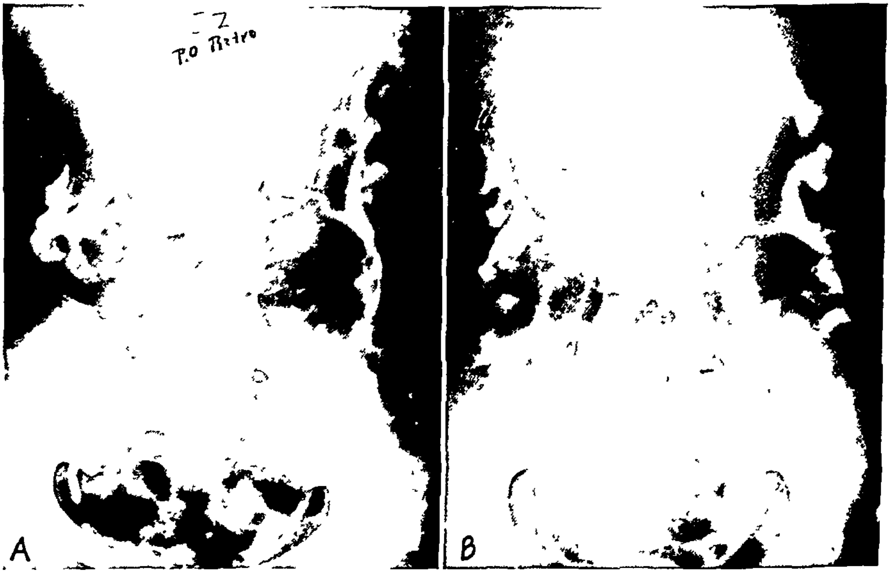

FIG 2 Case 1. *A*, preoperative retrograde pyelograms showing distortion of left calyceal system suggestive of polycystic disease and compression and rotation of right calyceal system. *B*, postoperative retrograde pyelogram showing reduction in renal size and improvement in calyceal structure.

After an uneventful recovery, he was discharged from the hospital on May 7, 1949, at which time hemoglobin was 12.5 gm., white blood cells 5,600 with 73 per cent neutrophils and blood urea nitrogen 16 mg. per cent. Excretory pyelograms showed reduction in size and improvement in calyceal structure of the right kidney.

The patient was readmitted June 15, 1949 without complaints and blood pressure of 150/90. On laboratory examination the hemoglobin was 12.6 gm. per cent; blood urea nitrogen 21 mg. per cent; urea clearance 50 per cent; phenolsulfonphthalein excretion 45 per cent in 2 hours; and urinalysis showed specific gravity 1.010 with a few white blood cells, while the culture was sterile.

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Phenolsulfonphthalein excretion 38 per cent with 16 per cent in first half hour; Mosenthal test showed concentration to 1.018; urea clearance 67 per cent; and urine culture was sterile.

On March 15, 1949, decompression of left polycystic kidney was performed. Again the postoperative course was smooth. Penrose drains were removed on fourteenth postoperative day. He was discharged April 12, 1949, at which time the blood urea nitrogen was 19 mg. per cent, urea clearance 76 per cent. Phenolsulfonphthalein 55 per cent excretion in 2 hours. The urine was negative and culture was sterile.

On follow-up examination January 16, 1950, he had no complaints, neither kidney was palpable; the blood pressure was 140/80, and the laboratory studies were: urea clearance 86 per cent, blood urea nitrogen 17 mg. per cent. The phenolsulfonphthalein excretion was 45 per cent and Mosenthal test revealed concentration to 1.017. A plain x-ray and excretory urogram showed marked reduction in the size of the kidney masses and improvement in pelvic and calyceal structure (fig. 3, *B*).

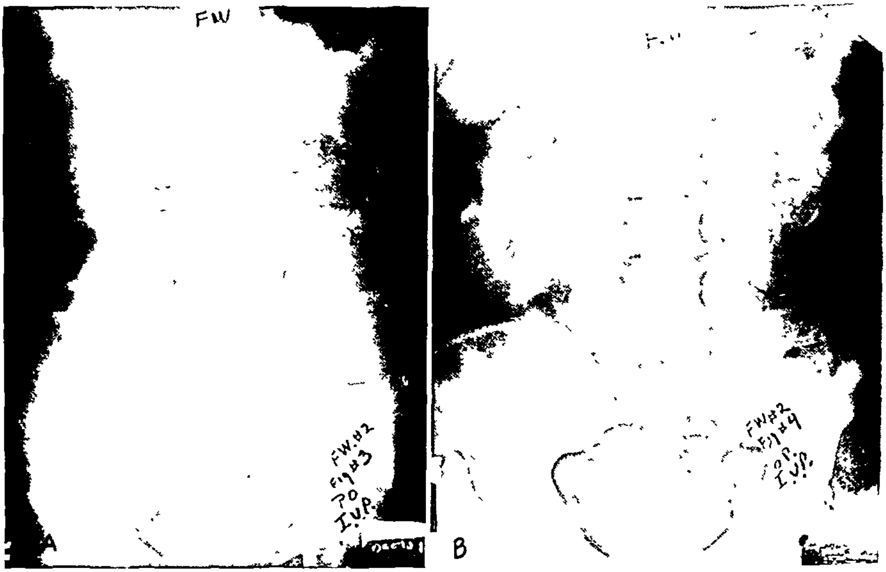

FIG. 3. Case 2. *A*, preoperative excretory urogram showing distorted calyceal system and enlarged renal shadows typical of polycystic renal disease. *B*, postoperative excretory urogram showing improvement in calyceal structure.

Case 3. A. F., a 46-year old white woman, was admitted July 24, 1948 to the Medical College of Virginia Hospital because of bilateral polycystic renal disease. In 1948, she had consulted a physician because of recurrent right lower quadrant abdominal pain, right flank pain of 5 years' duration and palpable abdominal masses. Exploratory laparotomy had revealed bilateral polycystic renal masses and she was referred for urological study and treatment.

She had been suffering from hypertension for several years with the systolic blood pressure ranging to 200 mm Hg. In January 1948, she had a subarachnoid hemorrhage and was comatose for 3 days. One sister died at 39 years of age of "tumor of the abdomen."

Examination revealed that the blood pressure was 150/100. Nodular upper abdominal masses extending 10 cm. below each costal margin and into the flanks were present. Urinalysis: Acid reaction, specific gravity 1.011; microscopic 6–8 white blood cells. The nonprotein nitrogen was 44 mg. per cent. The phenolsulfonphthalein excretion was 38 per cent in 2 hours with 25 per cent in the first half hour; urine culture was sterile. Retrograde pyelograms were typical for polycystic renal disease (fig. 4, *A*).

Surgical decompression of a markedly enlarged left polycystic kidney was performed July 26, 1948, under intravenous sodium pentothal and local novocain

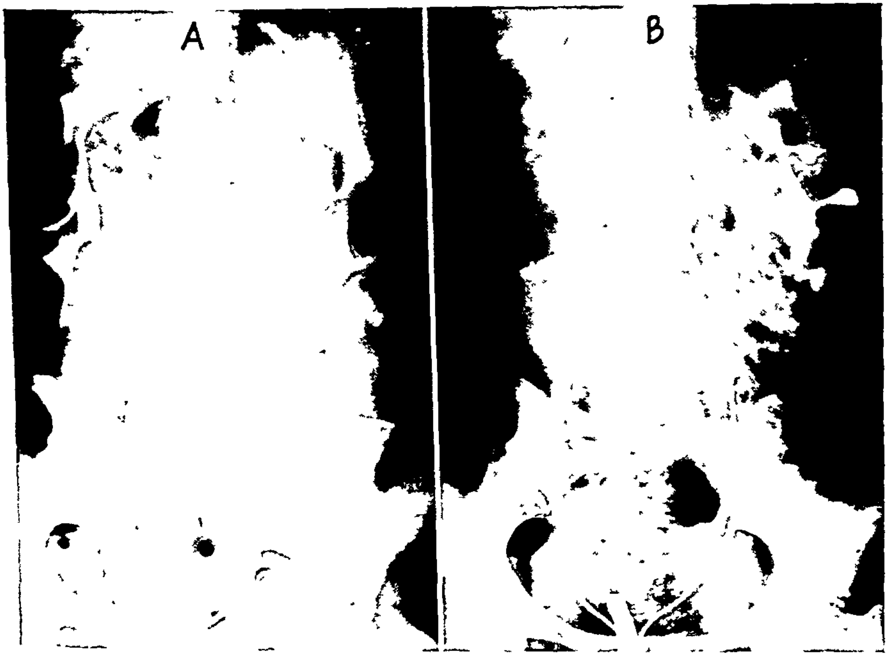

FIG. 4. Case 3. *A*, preoperative retrograde pyelograms. *B*, postoperative retrograde pyelograms showing reduction in renal size and improvement in calyceal structure.

anesthesia. The incision was closed after placing seven Penrose drains into the larger cysts and about the renal surface. The postoperative course was smooth. She was placed on penicillin 250,000 units daily. The Penrose drains were removed on the thirteenth postoperative day. On August 9, 1948, the nonprotein nitrogen was 30 mg. per cent and phenolsulfonphthalein excretion 38 per cent in 2 hours with 17 per cent in the first half hour. The blood pressure had become stabilized at 140 80. She was discharged August 11, 1948, the seventeenth postoperative day.

She was readmitted to the hospital November 8, 1948. At this time the left upper quadrant abdominal mass was barely palpable while the right upper quadrant mass was considerably enlarged over the previous admission. The blood pressure was 190/90. Laboratory studies showed: nonprotein nitrogen 31 mg. per cent. Urinalysis: Acid reaction, specific gravity 1.011, 2–3 white blood cells.

Decompression of the right polycystic kidney was performed November 10, 1948 under intravenous sodium pentothal anesthesia. She was again placed on 400,000 units of penicillin daily and the postoperative course was smooth. The Penrose drains were removed on the eleventh postoperative day. Retrograde pyelograms on November 22, 1948 showed marked reduction in renal size and improvement in calyceal structure (fig. 4, *B*).

Differential renal cultures were sterile and phenolsulfonphthalein excretion was 41 per cent in 2 hours with 18 per cent in the first half hour. She was discharged November 23, 1948 on the thirteenth postoperative day at which time the blood pressure was 120/70.

On postoperative follow-up examination on January 4, 1950 she complained of a constant, dull pain in the right upper quadrant and a small mass which moved with respiration was palpable in the right upper quadrant. The blood pressure was 130/80. Urinalysis showed specific gravity 1.012. The nonprotein nitrogen was 41 mg. per cent, and the phenolsulfonphthalein excretion 58 per cent in 2 hours with 22 per cent in the first half hour.

The right kidney was explored on January 5, 1950, under spinal anesthesia and a cyst 6 cm. in diameter of the anterior surface evacuated and unroofed.

The postoperative course was uneventful and she was discharged January 18, 1950.

*Case 4.** Mrs. J. T. C., a 36-year old white woman, was admitted to Dr. A. I. Dodson's service February 22, 1945, because of low back pain, nausea, and vomiting. Since adolescence she had suffered with "kidney colic" at intervals of 3 to 4 months to 2 to 3 years. The present attack began 3 weeks earlier when she was hospitalized and relieved of pain by ureteral catheter drainage. One week after discharge from the hospital there was recurrence of the discomfort accompanied by acute tenderness in the left flank and left upper abdomen.

The patient was a well-developed young woman who showed the effect of her 3 weeks' illness by considerable weight loss, pallor, and general weakness. Physical examination was essentially normal except for tenderness in each subcostal area and upper abdominal quadrants. Generalized rigidity of the abdominal muscles prevented satisfactory palpation of the kidneys, but there was fullness in both flanks.

The admission temperature of 100 rose to 103F within a few hours. Blood studies revealed: 3.7 million red blood cells, hemoglobin 57 per cent, and 16,000 white blood cells with 81 per cent neutrophils. The urine was acid, with specific gravity varying from 1.010 to 1.012 and contained a heavy trace of albumin and numerous red blood cells and pus cells. The phenolsulfonphthalein elimination was 35 per cent in 2 hours.

On cystoscopic examination indigo carmine was eliminated in poor concentration from both kidneys in 5 minutes. Catheterized specimens from both kidneys contained many pus cells and cultures were positive for E. coli. Pyelograms showed distortion of the pelves and calyces characteristic of cystic change (fig. 5, *A*).

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* Previously reported Journal of Urology, 57: 209–212, 1947.

Exploration of the left kidney was performed on February 28, 1945, under inhalation ether and ethylene anesthesia. A large abscess of the upper pole was evacuated and drainage tubes inserted. Several large cysts were evacuated and unroofed and drainage tubes inserted into each.

The postoperative course was satisfactory until March 9, when she complained of left flank pain and her temperature rose to 103F. Left flank pain and daily temperature elevations to 103F continued until March 17, 1945 when the left kidney was re-explored under ethylene inhalation anesthesia. Several additional cysts of the left kidney were evacuated, drainage tubes placed into each and the wound closed in layers.

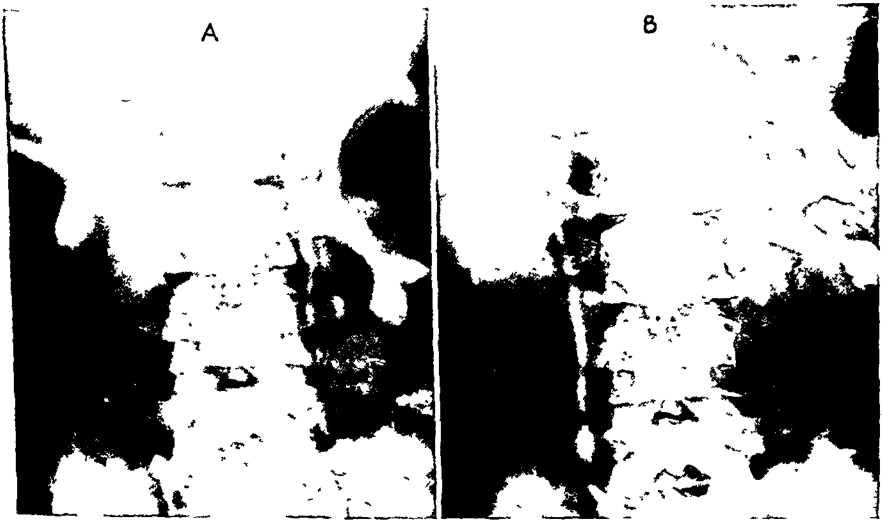

FIG. 5. Case 4. *A*, preoperative pyelograms showing calyceal structure typical of polycystic renal disease. *B*, postoperative pyelograms showing improvement of calyceal structure.

The left flank discomfort was relieved, but daily temperature elevation to 102F persisted and she complained of pains and tenderness in the right lumbar area. On March 27, the right kidney was explored under ether and ethylene anesthesia. Many cysts of the kidney were evacuated and unroofed and drainage tubes placed into each.

Postoperative improvement was gradual, the temperature subsiding to normal by April 5. During her hospitalization she was given 3 blood transfusions and on discharge from the hospital on April 14, 1945 she was in good condition, free of pain, and both wounds were well healed.

On postoperative evaluation May 29, 1945 the hemoglobin was 64 per cent with 3.4 million red cells. The urine contained 15 to 20 pus cells with specific gravity of 1.011. The phenolsulfonphthalein excretion was 55 per cent in 2 hours with 10 per cent in first, 30 per cent in second, 10 per cent in third and 5 per cent in the fourth half hour. Pyelograms indicated relief of pressure on the calyces (fig. 5, *B*).

She was readmitted to the hospital May 22, 1947 stating that she had been well and gained weight over a period of two years, but that in the week previous to admission had developed right flank pain followed by chills, temperature elevation and gross hematuria. On admission, temperature was 102F and there was tenderness in the right flank. Neither kidney was palpable and the blood pressure was 120/80. The nonprotein nitrogen was 38 mg. per cent; blood count hemoglobin 62 per cent with 3.3 million red blood cells, 17,500 white blood cells with 88 per cent neutrophils; urine alkaline, specific gravity 1.010, many white blood cells and red blood cells. Culture of the urine yielded E. coli.

On penicillin and forced fluids the temperature subsided to normal by May 25, but the right flank tenderness persisted. On May 27, 1947, the right kidney was explored under ethylene and ether anesthesia. Several abscesses appearing to be infected cysts were evacuated and rubber drains were placed into the cavity of each.

The maximum postoperative temperature elevation was 101F and on streptomycin and penicillin this subsided to normal by May 30. The postoperative course was smooth, the drains were removed on the twelfth postoperative day and the patient discharged on June 11, 1947.

Since that time she has been comfortable and there have been no further febrile episodes.

Case 5. L. W., a 37-year old white man, was admitted to McGuire Veterans Administration Hospital on January 15, 1948, complaining of left flank pain and gross hematuria. He was symptom free until 1941 when at 30 years of age he fell, striking his left side, suffering intense left flank pain with gross hematuria. After a month's hospitalization and repeated ureteral catheterizations and pelvic lavages the hematuria ceased. There had been several instances of gross hematuria and left flank pain between 1941 and 1948. The family history was of interest. His father and one uncle had died at 42 and 43 years of age of "kidney trouble." Two brothers and one sister had died at ages ranging from 31 to 43 years of "kidney trouble."

Examination revealed a poorly nourished and developed 37-year old white man. The blood pressure was 150/100. There was tenderness in the left flank and left upper abdominal quadrant, but no masses were palpable. Laboratory studies: Urinalysis showed trace of albumin, specific gravity 1.011, microscopic 10–20 red blood cells and 18–20 white blood cells, blood urea nitrogen 24 mg. per cent. CO_2 50 volumes per cent. The phenolsulfonphthalein excretion was 28 per cent in 2 hours with 5 per cent excretion in the first half hour, and Mosenthal concentration revealed a specific gravity of 1.013.

A plain x-ray revealed a calcific density overlying the lower pole of the left kidney 1.5 cm. in diameter and markedly enlarged renal shadows. An excretory urogram was suggestive of polycystic kidneys and was confirmed by retrograde pyelography. At time of retrograde studies indigo carmine was excreted in 10 minutes from the left kidney, but failed to concentrate beyond a trace. On the right, there was no excretion within 20 minutes (fig. 6).

Surgical decompression of the left polycystic kidney was performed under spinal anesthesia on February 5, 1948. The blood pressure varied from 160/100 to 80/60 during the procedure and in spite of infusion of 1000 cc blood and vaso-pressors the blood pressure was maintained with difficulty.

Immediately postoperative the blood pressure dropped to 80/40 and remained lowered for 6 hours even though intensive therapy was undertaken. The temperature was elevated to 101F on the first postoperative day, but subsided to normal on the sixth postoperative day on penicillin, sulfadiazine and intravenous fluids. However, on tenth postoperative day, it was again elevated and by the sixteenth day reached 103F. The urine was grossly purulent and E. coli grew on culture. The hemoglobin was 16 gm., white blood cells 14,450 with 87 per cent neutrophils, blood urea nitrogen 44 mg. per cent. The urinary output ranged between 2000–3000 cc daily. He developed nausea and vomiting with slight abdominal distention, and a mass was palpable extending 4 cm. below the right costal margin. On the eighteenth postoperative day the left flank incision was reopened and 200 cc hemolyzed blood evacuated, but the temperature continued to spike to 102F. On March 9 ureteral catheterization revealed 40 cc retention of very purulent urine in the right kidney which on culture yielded E. coli, and the catheter was left indwelling. However, the temperature continued to range from 101F to 103F. By March 17, the right upper quadrant mass extended down to umbilicus and into the flank and was quite tender. The right flank was explored on March 18, under spinal anesthesia, revealing a large perinephric abscess apparently originating from the rupture of a large cyst at the lower pole of a polycystic kidney. In spite of transfusions, infusions, and antibiotics, now including streptomycin, the temperature continued elevated and the course was downhill. By March 23 the urinary output dropped to 500 cc and the blood urea nitrogen 106 mg. per cent. He expired March 29, 1948.

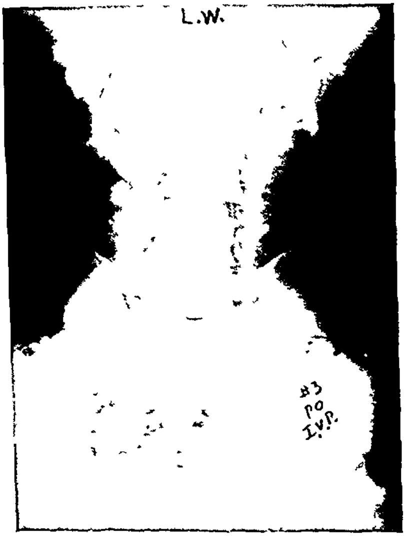

Fig. 6 Case 5 Preoperative excretory urogram

Autopsy report (Dr. Simon Russi): The peritoneal cavity contained 3000 cc of clear, straw colored fluid. A nodular, cystic mass filled the right retroperitoneal space extending from the diaphragm to the iliac crest and medially beyond the midline. The left kidney was 3 times normal size. The right kidney weighed 3850 gm. and measured 30 by 18 by 11 cm. The surface was studded with cysts varying from a few millimeters to 6 cm. in diameter. On sectioning, the kidney was honeycombed with cysts of varying size which had replaced all normal appearing renal tissue. About one third of the cysts were grossly infected. The pelvis and calyces were elongated and distended. The left kidney was similar to the right except that it was much smaller and did not show so much gross infection.

Case 6. W. R. S., a 37-year old white man, was admitted to McGuire Veterans Administration Hospital on April 1, 1948, complaining of shortness of breath and back pain. Several years previously he had noted upper abdominal enlargement which gradually increased. Examination revealed flaring of the lower thoracic cage and upper abdominal fullness. Soft nodular masses were palpable from the costal margin to the iliac crests and from within 4 cm. of the midline to the flanks. These moved with respiration. The blood pressure was 150/110.

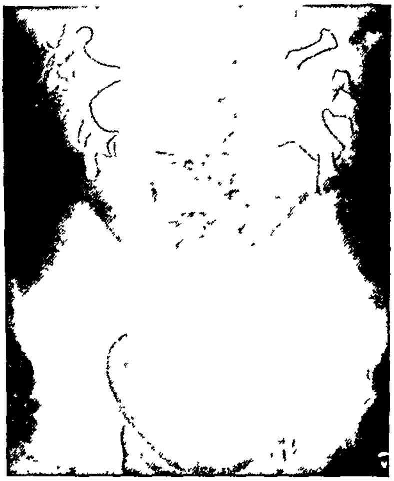

FIG. 7. Case 6. Preoperative excretory urogram

Laboratory studies: Blood urea nitrogen 32 mg. per cent. Blood proteins 7.5 gm. per cent with albumin 4.7 gm. and globulin 2.8 gm. Urinalysis: Reaction acid, specific gravity 1.012, albumin trace; microscopic, 3–5 white blood cells and red blood cells. The phenolsulfonphthalein output was 15 per cent in 2 hours with only a trace in first half hour; Mosenthal showed concentration to 1.013; urine culture showed no growth. A plain x-ray and an excretory urogram showed markedly enlarged renal shadows and contrast medium outlined the calyceal system as typical polycystic kidneys (fig. 7).

Surgical decapsulation and decompression of a markedly enlarged left polycystic kidney was performed April 9, 1948 under spinal anesthesia. Although 1000 cc of blood was given during the procedure, the blood pressure dropped from an initial 130/80 to 80/50. At the termination of surgery the blood pressure was 120/80, but dropped to 80/30 shortly thereafter and was not elevated until 8 hours later to 110/70.

Postoperatively he received penicillin and sulfonamides. The temperature rose to 101F, but subsided to normal by the seventh postoperative day. The urinary output ranged from 1500 to 2900 cc daily, and he was out of bed in a chair on the fifth postoperative day. The Penrose drains were removed on the fourteenth postoperative day. On the sixteenth postoperative day the temperature was elevated to 101F and laboratory studies showed: white blood cells 25,300 with 86 per cent polymorphonuclears; blood urea nitrogen 40 mg. per cent, urine 1-3 white blood cells, specific gravity 1.012, and urine culture was negative.

Temperature continued elevated and by May 19 reached 102.6 at which time the urine was loaded with pus and left flank distention was noted. Under local anesthesia, the left flank incision was reopened and considerable thick creamy pus evacuated from the perirenal space. At this time streptomycin was obtained and he was given 3 gm. daily in divided intramuscular doses. Abdominal distention developed and was unrelieved by Wangensteen suction. Although the urinary output remained from 1200 to 2300 cc daily with specific gravity of 1.006 to 1.012, the blood urea nitrogen gradually rose to 120 mg. per cent, and he expired June 1, 1948. Autopsy was not permitted.

DISCUSSION

In the past polycystic renal disease has been considered by most authorities to be a hopeless progressive disease best treated by medical measures. Surgical attack has been advised only when necessitated by complications. We believe surgical decompression should be considered in carefully selected cases which show early impairment of renal function, in an effort to prevent progression of this impairment. Since the average age at death in polycystic renal disease is 50 years, these unfortunate individuals should be offered the opportunity of greater longevity if possible. Surgical decompression seems to offer this opportunity. In four of the patients reported there was reduction in size of the renal mass, improvement in the calyceal structure, improvement in the renal function, and reduction of an elevated blood pressure.

Two instances of fatal termination are reported. This may seem unduly high for a small series of 6 operative cases. However, had the present day antibiotics (streptomycin, aureomycin and chloromycetin) been available the postoperative infection might have been more readily controlled and a successful result obtained. Also, mistakes were made in selection and handling in these instances. Case 6, W. R. S., showed considerable reduction in renal function as evidenced by blood urea nitrogen of 32 mg. per cent and phenolsulfonphthalein excretion of 15 per cent in 2 hours. Here surgery was probably ill advised. In case 5, L. W., elevation of the kidney rest at operation probably ruptured cysts of the dependent kidney with a resultant spreading perinephric infection which was belatedly recognized. Earlier recognition of this complication may have meant a happy termination. In both instances, selection of spinal anesthesia may have been our downfall, since there was a drop in blood pressure during operation which was not restored to normal for from six to eight hours. Recent work on electrolytic balance of sodium and potassium levels in uremic states has been encouraging. Determination and correction of electrolytic imbalance in these two instances may have prevented a fatal outcome after the postoperative infection was controlled.

SUMMARY AND CONCLUSIONS

The incidence, etiology, symptoms, and signs of polycystic renal disease are discussed.

In properly selected cases of polycystic renal disease bilateral decompression of the kidneys may result in improvement of renal function and prolongation of life.

Failure in the past has probably been due to the improper selection of cases and uncontrolled postoperative infection.

Six operative cases are reported with definite improvement in renal function and pyelograms in four.

The pre- and postoperative treatment and operative technique are discussed with emphasis placed on the use of antibiotics, selection of anesthesia, proper operative positioning of the patient and sufficient wound drainage.

REFERENCES

Bobbitt, R. M.: J. Urol., **50:** 131–140, 1943.
Braasch, W. F. and Hendrick, J. A.: J. Urol., **51:** 10, 1944.
Cahill, G. F. and Fish, G. W.: Trans. Amer. Assoc. of G.U. Surg., **34:** 81, 1941.
Dodson, A. I.: J. Urol., **57:** 209–212, 1947.
Goldstein, A. E.: J. Urol., **34:** 536–548, 1935.
Goldstein, A. E. and Klotz, Ben: Surgery, **6:** 730–746, 1939.
Hausman, H.: Am. J. Surg., **49:** 335–341, 1940.
Kohler, B.: Acta Chir. Scandinav., **96:** 283–295, 1948.
Lambert, P. P.: Arch. Path., **44:** 34–58, 1947.
Lockwood, J. S. and Werner, S. C.: Surgery, **26:** 341–361, 1949.
Melicow, M. M. and Gile, Harold H.: J. Urol., **43:** 767–773, 1943.
Norris, Robert F. and Herman, L.: Trans. Amer. Assoc. of Genito-Urin. Surg., **31:** 41–57, 1938.
Randall, H. T., Habif, D. V., Lowsley, O. S. and Curtis, M. S.: J.A.M.A., **127:** 1112–1119, 1945.
Rathbun, N. P.: Trans. Amer. Assoc. Genito-Urin. Surg., **35:** 131–145, 1942.
Reaves, J. U.: South Surg., **11:** 254–265, 1942.
Ridlon, G. R.: J. Urol., **46:** 480–485, 1941.
Rolnick, H. C.: J. Urol., **47:** 648–650, 1942.
Roos, A.: Am. J. Dis. Child., **61:** 116–127, 1941.
Stevens, A. R.: J. Urol., **52:** 430–436, 1944.
Walters, W. and Braasch, W. F.: Surg., Gynec. & Obst., **58:** 647–650, 1934.
Whitmore, E. R.: Cysts of the kidney. South Med. J., **31:** 118–129, 1938.
Yardumian, K. Y. and Ackerman, M. A.: Urol. & Cutan. Rev., **47:** 147–150, 1943.
Young, W. W.: J. Urol., **55:** 323–329, 1946.

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DISCUSSION

Dr. Albert E. Goldstein (Baltimore, Md.): Probably every man in this room has been confronted at one time or another with a case of polycystic disease and wondered just what to do about it. There certainly is diversity of opinion, not only among general physicians but among urologists, as to what to do, and I believe it is because of the diversity of opinion that the authors bring this before you. I am very happy that they have. Their purpose in their discussion was to relieve the individual of the pressure of the cyst to prevent further damage. They have accomplished this in numbers of cases.

We have not had any experience in our cases with sclerosing solutions but, in addition to what they have done in their cases, we have gone much further. We believe that more radical surgery is necessary than just opening the cyst and extracting whatever secretion there may be in the large cyst and unroofing the top of the cyst, because you must remember, to begin with, no one should be under the impression that in polycystic disease, no matter what you do in these cases, you are going to cure the patient. There isn't any such thing as a cure, so we must start with that particular premise, that you are going to relieve. Your only hope is to relieve pain, to improve the general condition of the patient, to prolong life and to rehabilitate the individual so that he can go about his business whenever possible.

As I say, they have accomplished this, and we have gone much further. We are sure (and I believe the essayists are of the same opinion) that these cysts are going to reform, and not only reform but there are small cysts that you encounter at the time of the operation that you cannot do anything about. What are you going to do; are you going to operate on this patient every time he has pain because of the enlargement of the cyst or because of the increase in urea? Something must be done because you cannot expose that kidney each time, so we devised and suggested a method in 1935 that we have carried out now in 28 cases.

(Slide) This is an actual drawing of one of our cases, the first case, in reality, showing the cysts as presented. We have done it extraperitoneally—either abdominally or lumbar. The selection of the site depends on certain conditions.

You see here the number of cysts. We aspirate. In 1935, we aspirated as much as we could, and in some cases we aspirated as much as 1100 and 1200 cc, but that was a mistake. As we went along later on, we found that, when we took out more than 400 to 500 cc, the patient went into shock, so now when we perform the operation, we never aspirate over 400 to 500 cc, and then we can continue on at another date through another method.

With the exposure of this kidney and the aspiration made of the large cysts, we then split the kidney lengthwise from stem to stern, because there are other cysts exposed as you aspirate these, and as there is a reduction in the size of the surface of the whole kidney, particularly on the surface, we see other cysts, so we split the kidney all the way down to the calyces. One must try not to get into the calyces or pelvis of the kidney because then you get a temporary urinary tract fistula. We do not want urinary tract fistulas as it causes delayed healing and extra hospitalization.

(Slide) With that kidney split as I mentioned (and you will see there the cysts have been aspirated), there are other cysts that are found and they are aspirated. This is split down to the calyx. After that, we take through-and-through sutures from the cortex of the kidney, through the muscle, through the fascia, through the fat, through the skin, using about four sutures on each side, on both sides, and the kidney is left wide open in this fashion (indicating), because urinary drainage will continue after the operation.

(Slide) This is what happens after about four to five weeks following the operation. You get a scar that looks like this. As I say, the wound is left open to allow for further secretion, and this (indicating) is the scar. It is important that you bring this kidney up to the surface of the skin. Following this, one may have to aspirate at a subsequent time and go through the scar.

We found that this procedure was a very valuable procedure. We operated on 28 cases. To prove to ourselves whether there was any value in it, we took 36 unselected cases in the last 9 years and operated upon them alternately; in other words, we did not select the cases but operated upon 18 and did not operate upon the other 18, and to sum the thing up (it will be reported shortly*), we have found that the patients who were operated upon lived two-and-a-half times longer than those who were not operated upon. This, to me, is a definite demonstration that there is value in operating on these cases but you must do radical surgery to them because the cysts must be punctured again and there is no use exposing the kidney at another time.

I think the operative procedure is certainly worthy of consideration and I want to compliment the authors for the fine piece of work they have done.

Dr. C. Van Cappellen (Amsterdam, Holland): It has been well established that at autopsy examination of patients with polycystic disease, the cysts have been found under rather high pressure. Upon opening them we were sure to find a jet of clear fluid come out of the cysts. I have seen many patients with polycystic kidneys but it was not until March 1950, that I operated upon my first case.

This patient was a man of 39 years. In a well kept family history dating back to 1814, death from kidney trouble was usual. Familial polycystic disease was well recognized in this family. Fifty-two years was the maximum that any of the family who had developed kidney trouble had lived.

You can all imagine with what dread this intellectual man of 39 received this diagnosis. The diagnosis was easily made due to the large palpable kidney and the cystoscopic and x-ray findings.

The blood pressure was 230 over 130. The heart was enlarged to the left. There was no cardiac insufficiency. The urine was clear, albumin a trace, pus cells 10, red blood cells 6, urea clearance 45 per cent, blood urea 48 mg. per cent.

First operation (left kidney) March 15, 1950: Many large cysts were widely opened and as far as possible the walls of the cysts were resected. Ten days following the first operation the blood pressure had dropped to 190 over 110. The blood urea was 32 mg. per cent and the urea clearance had increased to 64 per cent. A trace of albumin was still present in the urine.

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* August issue, J. Urol.

Second operation, March 27: Same findings as in the left kidney. After operation on April 4 the blood urea was down to 22.5 mg. per cent and the urea clearance had risen to 71 per cent. The blood pressure was 170 over 90. The urine was negative.

When the patient left the hospital a month after his first operation he felt fit and was anxious to continue with his work. Before operation he was not able to carry on with his employment.

The future will decide if we are to continue with this type of operation. When is the best time to operate? In my opinion this should be done as early as possible.

A second patient, in a much later stage of the disease, developed a considerable reaction to operation. The blood urea rose to 150 mg. per cent. It afterwards fell to 75 mg. per cent. We did this operation when the urea was 58 mg. per cent.

In my opinion we must not operate on a too advanced stage of the disease.

Dr. W. W. Young (Watertown, N. Y.): Although my experience in the surgical treatment of polycystic disease is extremely limited, I feel both obligated and privileged to commend highly the authors of this paper for their fine presentation and study and their efforts to preserve renal function in this disease which has been considered so hopeless by so many.

Anyone advocating surgical treatment for uncomplicated polycystic renal disease leaves himself wide open for considerable criticism. I believe that the authors of this paper are here today carrying the torch for those of us who believe that the surgical approach to this problem does offer a means of preserving and improving renal function, and of prolonging life when used before renal function is badly impaired or complications occur.

Fundamentally, in addition to the exact technique which the authors have presented, there are available at the present time three procedures or methods of surgically treating uncomplicated polycystic renal disease. These are, of course, the older method of Rovsing, who in 1910 advocated multiple puncture of the cysts. This is essentially the method used by the authors in this paper, to which they have added the use of Zenker's solution, as suggested, I believe, by Dr. Dellinger Barney for solitary cysts as a sclerosing agent applied directly to the exposed lining of the cystic cavities.

Then there is the marsupialization procedure of Dr. Goldstein, with which you are all familiar.

Thirdly, there is the procedure which we used some years ago and reported in the *Journal of Urology* (**55**: 323, 1946), in a paper entitled "Sclerosing Injection of Polycystic Kidney Following Surgical Exposure." This method was used first on a young woman 17 years of age, with a huge and rapidly enlarging left polycystic kidney. This kidney was exposed with the usual oblique lumbar incision and both preoperatively and during the operation indigo carmine was given intravenously as a means of enabling us to differentiate the cystic cavities from tract fistula. We do not want urinary tract fistulas as it causes delayed healing and extra hospitalization.

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When the patient left the hospital a month after his first operation he felt fit and was anxious to continue with his work. Before operation he was not able to carry on with his employment.

The future will decide if we are to continue with this type of operation. When is the best time to operate? In my opinion this should be done as early as possible.

A second patient, in a much later stage of the disease, developed a considerable reaction to operation. The blood urea rose to 150 mg. per cent. It afterwards fell to 75 mg. per cent. We did this operation when the urea was 58 mg. per cent.

In my opinion we must not operate on a too advanced stage of the disease.

Dr. W. W. Young (Watertown, N. Y.): Although my experience in the surgical treatment of polycystic disease is extremely limited, I feel both obligated and privileged to commend highly the authors of this paper for their fine presentation and study and their efforts to preserve renal function in this disease which has been considered so hopeless by so many.

Anyone advocating surgical treatment for uncomplicated polycystic renal disease leaves himself wide open for considerable criticism. I believe that the authors of this paper are here today carrying the torch for those of us who believe that the surgical approach to this problem does offer a means of preserving and improving renal function, and of prolonging life when used before renal function is badly impaired or complications occur.

Fundamentally, in addition to the exact technique which the authors have presented, there are available at the present time three procedures or methods of surgically treating uncomplicated polycystic renal disease. These are, of course, the older method of Rovsing, who in 1910 advocated multiple puncture of the cysts. This is essentially the method used by the authors in this paper, to which they have added the use of Zenker's solution, as suggested, I believe, by Dr. Dellinger Barney for solitary cysts as a sclerosing agent applied directly to the exposed lining of the cystic cavities.

Then there is the marsupialization procedure of Dr. Goldstein, with which you are all familiar.

Thirdly, there is the procedure which we used some years ago and reported in the *Journal of Urology* (**55**: 323, 1946), in a paper entitled "Sclerosing Injection of Polycystic Kidney Following Surgical Exposure." This method was used first on a young woman 17 years of age, with a huge and rapidly enlarging left polycystic kidney. This kidney was exposed with the usual oblique lumbar incision and both preoperatively and during the operation indigo carmine was given intravenously as a means of enabling us to differentiate the cystic cavities from the renal pelvis and calyces. We then proceeded to aspirate the larger individual cysts with ordinary Luer syringes and needles, and to reinject each cyst, before removing the needle, with 1 cc of sodium morrhuate to each 10 cc of cystic fluid removed.

I hold no brief for sodium morrhuate; there are probably other sclerosing solutions that may be better.

Of course, the smaller, surface cysts were simply punctured. The kidney decreased to almost half its original size. The postoperative convalescence was uneventful. There was no appreciable reaction to the sodium morrhuate that we could determine. The elevated blood pressure declined and the patient's incapacitating abdominal pain was relieved. She subsequently lived comfortably and asymptomatically for about five years, and died one month after giving birth, by cesarean section, to living, normal twins.

Prior to this time, during the 5-year period, she had given birth to another normal child.

Postmortem examination revealed the left kidney to be smaller than the right kidney, whereas at the time of the operation, the hugely enlarged left kidney was almost three times as large as the right kidney. This was observed after five years.

Any one of these procedures which we have mentioned can be used alone or in combination with the others. All are designed to preserve renal function by removing as many multiple, intruding cystic masses as possible. Our sclerosing technique has only been reported, to my knowledge, in one other case. The result in this instance was apparently successful.

I think the authors have adequately shown by their work that surgical decompression in properly selected cases—and that, of course, is most important—definitely improves renal function. I feel strongly that these decompression procedures should be reserved for uncomplicated polycystic disease. Patients with relatively good renal function who are asymptomatic should certainly not be subjected to surgery, but those patients who, under careful observation, show a definitely declining renal function, or who develop pain or appreciable hematuria or hypertensive symptoms, may be immeasurably benefited by a decompression operation if carried out before infection and other complications occur. I would certainly encourage the authors to carry on with their good work and I hope their achievement will stimulate others to follow in their footsteps.

DR. JAMES A. SEAMAN* (Springfield, Mass.): This is a curious subject which the authors have brought up and have discussed so admirably. I know of nothing more interesting in urology than that pathologically beautiful kidney which is like the tropical birds that are so beautiful and do not sing. This beautiful bit of pathology does not function very well.

I have seen the marsupialization that Dr. Goldstein speaks of. It sounds intriguing. We know these cysts do recur. I have often wondered whether we ought not to puncture every little pinhead cyst. They occur in clusters all around the renal parenchyma. The big one is very easy to incise and paint with anything you want. I will do it, because I still think that some of those we do incise recur.

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* Deceased

Marsupialization seems to be one of the answers. I often do the Rovsing or some type of Rovsing operation, which I think is the answer. You have to do something. It is doubtful whether you will be subject to criticism if you take a kidney that is beginning to demonstrate itself as a polycystic kidney and operate upon it before real symptoms begin. Somebody, I think it was a German, told us that each kidney has about a million glomeruli. I wonder how many normal glomeruli there are in these kidneys that are tremendously compressed with cysts all over them. I wonder how many are left after you do a Rovsing operation or a marsupialization—I wonder how many normal glomeruli are left. I wish this same fellow who counted them before could tell us numerically how many glomeruli that are left are really functioning.

If we do not get all the cysts, we are going to be in trouble. I think each of these tiny pinhead things should be punctured. They are going to grow and as they grow around the pelvis they are going to give more obstruction.

Nobody has said anything about postoperative care, and I think somebody should. We are so likely to operate upon these patients and be satisfied that we have done a nice job. They get along well, lose that ashen gray color that so many of them have, the blood pressure drops, the renal function improves, all of which are very gratifying, but they get into more trouble if we do not follow them up. If we lose sight of any obstructive uropathy: kinks in the ureter, stones, prostates, a large bladder in the woman with a cystocele, strictures in the urethra, later difficulty may develop. With strictures of the ureter, I think one of the nicest things to do is to dilate these ureters periodically, if the patient begins to have symptoms, headache and whatnot. They will function better, the patient will feel better, the pain is lessened.

I will tell you one little story about a patient 75 years of age in an automobile accident who had a ruptured polycystic kidney. I punctured all the cysts, patched up his ruptured kidney, and then he went home in 2 weeks. Two months later, at home, his 7-year-old great-grandson came in playing Indian and he hollered, "Hey, Grandpa, I'll shoot you," and he picked up his brother's 22 rifle and fired it. The bullet ricocheted off two walls and went down and struck Grandpa in the heart and he dropped dead.

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THE RESULTS OF TREATMENT OF HYDRONEPHROSIS BY A PLASTIC SURGICAL PROCEDURE WITH AND WITHOUT T-TUBE DRAINAGE

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From the Department of Surgery, Section on Urology, Yale University School of Medicine and the Grace-New Haven Hospital, New Haven, Conn.

In order to conserve a hydronephrotic kidney some type of plastic surgical procedure is required to give the patient relief of discomfort and to maintain a normal functioning renal organ. The fact that numerous surgical operations are being advocated from various parts of the world would signify that no one plastic procedure has been accepted as the final surgical method for correction of hydronephrosis. The medical literature does not contain sufficient reports of careful long-time follow-up of each of a series of the better procedures to satisfy the urologists of today who wish to be apprised of the minute facts concerning the permanent anatomical, physiological, bacterial and symptomatic results of such plastic surgical procedures. To maintain normal renal function if present or to cause a reversible hydonephrosis to resume permanent normal function without any injury to the organ by incising its cortex or inducing an infection requires further surgical efforts. The ideal operation would be one which would produce a permanent and adequate ureteropelvic outlet, allow the kidney to maintain a normal physiological function free from infection and relieve the patient of all symptoms.

It is our purpose to describe an operation which we have used during the past seven years for the correction of ureteropelvic obstruction. We have not used this operation exclusively, but we wish to present our results in thirty consecutive cases. In our hands it has been more broadly applicable and more regularly successful than other techniques.

The technique is illustrated in figure 1. The kidney is approached by the usual lumbar extraperitoneal route. After the pelvis and ureter have been cleaned of adherent tissue, and after the operator ascertains the presence of stenosis at the ureteropelvic junction or in the upper ureter, silk traction sutures are placed at the upper and lower portions of the renal pelvis to mark the line of pelvic resection. These sutures aid materially in handling the pelvis and guide the operator while he is excising the redundant pelvic tissue. At this point the operator must determine that there will be sufficient length of ureter to make a tension-free anastomosis of the pelvis and ureter after the obstructed portion of the ureter is excised. If there is doubt about this it will be wise to preserve part of the extrarenal pelvis to construct a tube which will reach the cut upper end of the ureter without tension. Such an exigency will be rare and will arise only when there is a long stricture of the upper ureter. In the average case all redundant extrarenal pelvis is excised including the ureteropelvic junction and the stenotic upper ureter. The anterior and posterior cut edges of the pelvis are then sutured

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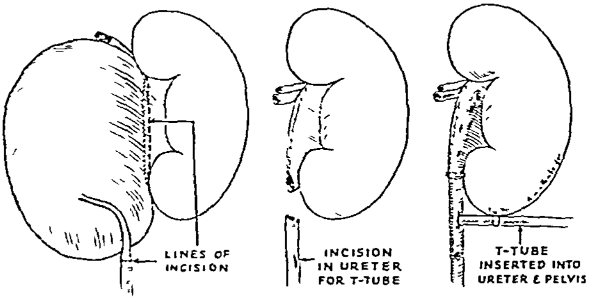
Read at annual meeting, American Urological Association, Washington, D. C., June 1, 1950.

together from above downward with a continuous inverting suture of 00000 chromic catgut. The lower end of this suture line is left open for a distance of 1 cm. and will be the site of anastomosis of the ureter and pelvis. The pelvic suture line is reinforced with interrupted sutures of the same material placed in the adventitial layer of fascia which one always finds closely surrounding the renal pelvis.

A vertical incision 1 cm. long is then made in the ureter 3 cm. below the cut end. Through this incision is inserted a latex T-tube of the largest size that will fit comfortably in the ureter. We have rarely used a tube smaller than 18F in the adult and 14F in the infant and child. This tube is cut and placed as illustrated so that a relatively long arm will extend upward into the renal pelvis and a shorter arm (2 cm.) downward into the ureter distal to the ureterotomy. A notch opposite the long draining stem of the tube is necessary to facilitate removal and to inspect the patency of the junction between the limbs of the "T". We have almost invariably found an incomplete diaphragm of latex at that site which must be cut away to provide adequate drainage through the tube. Failure to remove this diaphragm may result in obstruction and back pressure on the suture lines.


LINES OF INCISION
INCISION IN URETER FOR T-TUBE
T-TUBE INSERTED INTO URETER & PELVIS

PYELOURETEROPLASTY FOR HYDRONEPHROSIS WITH T-TUBE URETERAL DRAINAGE

FIG. 1.

The upper arm of the T-tube is inserted into the pelvis through the opening at the lower end of the pelvic suture line. The ureter is anastomosed to the lower end of the pelvic incision around the tube. Interrupted sutures of 00000 chromic catgut are used and are placed so as to evert the mucosa. Four to six such sutures will usually suffice. This suture line is reinforced with interrupted sutures of the same material in the adventitia of the ureter and pelvis.

The kidney is replaced in its fossa, particular care being taken to be sure that the ureter lies straight and unobstructed. If necessary a Deming nephropexy is done. The long draining limb of the T-tube is sutured with plain catgut to the capsule of the kidney at the lower pole to steady the position of the T-tube with respect to the kidney and ureter. The T-tube is brought out in the middle of the flank incision so that the patient will not kink the tube when he lies on his back. The perirenal space is drained with one medium-sized Penrose drain from which the wick has been removed. After the wound is closed, the tube is sutured to the skin with braided silk. It is important that the tube be secured in such a way that it is not kinked and does not push or pull on the ureter.

The T-tube is connected to a drainage bottle. The patient is given both sulfonamide and penicillin. We have not used the newer antibiotics in enough of these cases to determine their effects, but sepsis has not been a problem. Temperature elevation of significant degree for more than the first 3 days occurred in only 1 case due to a severe mixed infection of enterococcus and Pyocyaneus. The patients are allowed out of bed after the second postoperative day unless a nephropexy has been done.

On or about the seventeenth postoperative day the T-tube is injected with diodrast to outline the renal pelvis and ureter, and at that time the T-tube is withdrawn. We believe that the introduction of 1 or 2 cc sterile oil into the tube at the time of withdrawal facilitates its removal. We have never encountered any difficulty removing the tube and advise gentle steady traction until the tube is pulled into the drainage tract. The tube tract will usually drain a small amount of urine for twelve hours or less. The longest any of our cases drained urine was twenty four hours after removal of the tube. The drainage tract is usually healed within three days. We have never seen stricture develop at the point where the T-tube entered the ureter.

RESULTS

A careful follow-up for anatomical, functional and symptomatic results was inaugurated in each case. Urine examinations and excretory urograms were done prior to discharge from the hospital and were repeated at the end of 1 year, and the older ones have likewise been recently examined. Renal functional tests were estimated at the end of one year and later by ureteral collection of normal amounts of phenolsulfonphthalein or by the appearance of normal concentration of diodrast within 5 minutes of its intravenous administration. Twenty-seven of the 30 cases have good anatomical and functional results and are entirely relieved of their pain. Five of the thirty patients had this plastic procedure applied to their single kidney; all of these were completely successful from every point of view. In addition, 1 patient had bilateral lesions, both of which were treated successfully with T-tube splint and drainage.

Three secondary nephrectomies have been required because of continued infection and obstruction. Our first case with this operative technique was treated without splint or drain. Curiosity led to premature passage of a ureteral catheter into the renal pelvis on the sixteenth day after operation. Apparently this procedure dislocated the anastomosis, requiring removal of the kidney. The other two cases had an unusually long segment of narrowed ureter which was not wholly determined prior to operation. Consequently these anastomoses were closed under slight tension and with some misgiving. These failures are explicable and avoidable.

In most cases the urinary tract has cleared promptly of infection after removal of the tube. Patients who had infection longer than one month after leaving the hospital had Proteus, Pyocyaneus, enterococcus, or Aerobacter aerogenes infections or had poor anatomic results leading to nephrectomy. Twenty-three cases show perfect anatomical and functional results and have normal, uninfected urines. Eleven of the thirty cases came to us with infection. Eight cleared following operation. Three remain infected. One of the preoperatively uninfected cases is persistently infected postoperatively. This case is 5 months postoperative and has a Pyocyaneus infection which so far has been controlled but not cleared by chloromycetin. One is 18 months after operation with an Aerobacter aerogenes infection resistant to streptomycin and not yet treated with aureomycin or chloromycetin. The third case is 2½ years after operation with an enterococcus infection not yet exposed to the newer antibiotics. The fourth is 6 years postoperative and has a Proteus infection complicating a bladder neck contracture with residual urine. He has refused surgical treatment of the contracture. Apparently chronic pyelonephritis preoperatively compromises the chance of clearing the urine after operation. Perhaps the new antibiotics will simplify this problem.

TABLE 1. *Age distribution of 30 patients*

1 to 10 years	4
11 to 20	4
21 to 30	9
31 to 40	4
41 to 50	6
51 to 60	3

TABLE 2 *Length of time since operation for successful cases*

1 year and less	4
1 to 2 years	2
Over 2 years	21
Over 3 years	15
Over 5 years	11

The longest follow-up is 7½ years

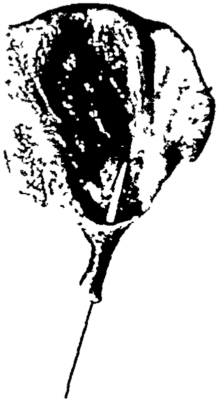


FIG 2. Specimen of extrarenal pelvis and ureteropelvic junction removed from case whose x-rays are shown in figure 3

See tables 1 and 2.

We have not seen progressive narrowing of the anastomosis or reduction of function later than one year after operation. All cases followed for 5 years or

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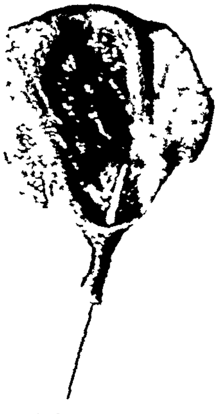

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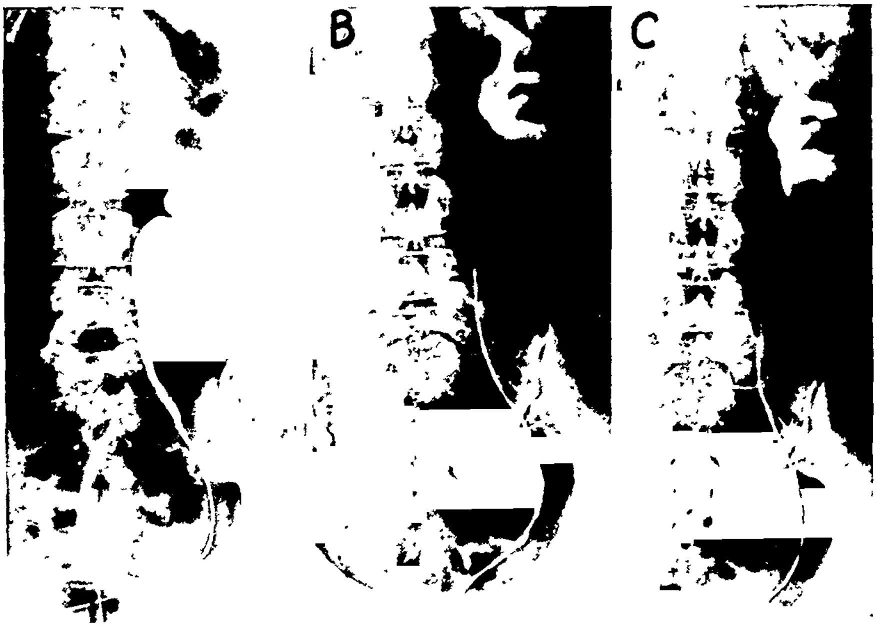

FIG. 3. A.W., 41 year old woman, N.H.H. Unit B 91106. Long period of left renal infection. *A*, retrograde pyelogram showing obstruction at left ureteropelvic junction associated with large aberrant artery to lower pole. *B*, retrograde pyelogram 1 year after operation. *C*, retrograde pyelogram 2 years after operation. Urine sterile. Each kidney now excretes 15 per cent PSP in 15 minutes with 2 minutes appearance time.

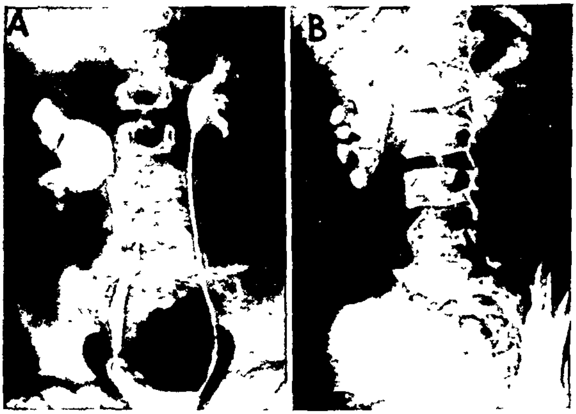

FIG. 4. J W., 3½ year old girl, N H.H. Unit C 12690. Repeated attacks acute pyelonephritis due to B. coli and enterococcus *A*, retrograde pyelogram showing obstruction at right ureteropelvic junction caused by intrinsic stenosis of upper 2 cm. of right ureter. *B*, right posterior oblique excretory urogram 1 year after operation Diodrast appears in good concentration in both kidneys on 5-minute film. Urine remains sterile. No further attacks of pain or fever.

more have excretory urograms or retrograde pyelograms which compare favorably with those taken shortly after operation. In some instances the 5-year pyelograms look better than those taken during the first year. The poor results have been obviously poor within the first 2 or 3 months.

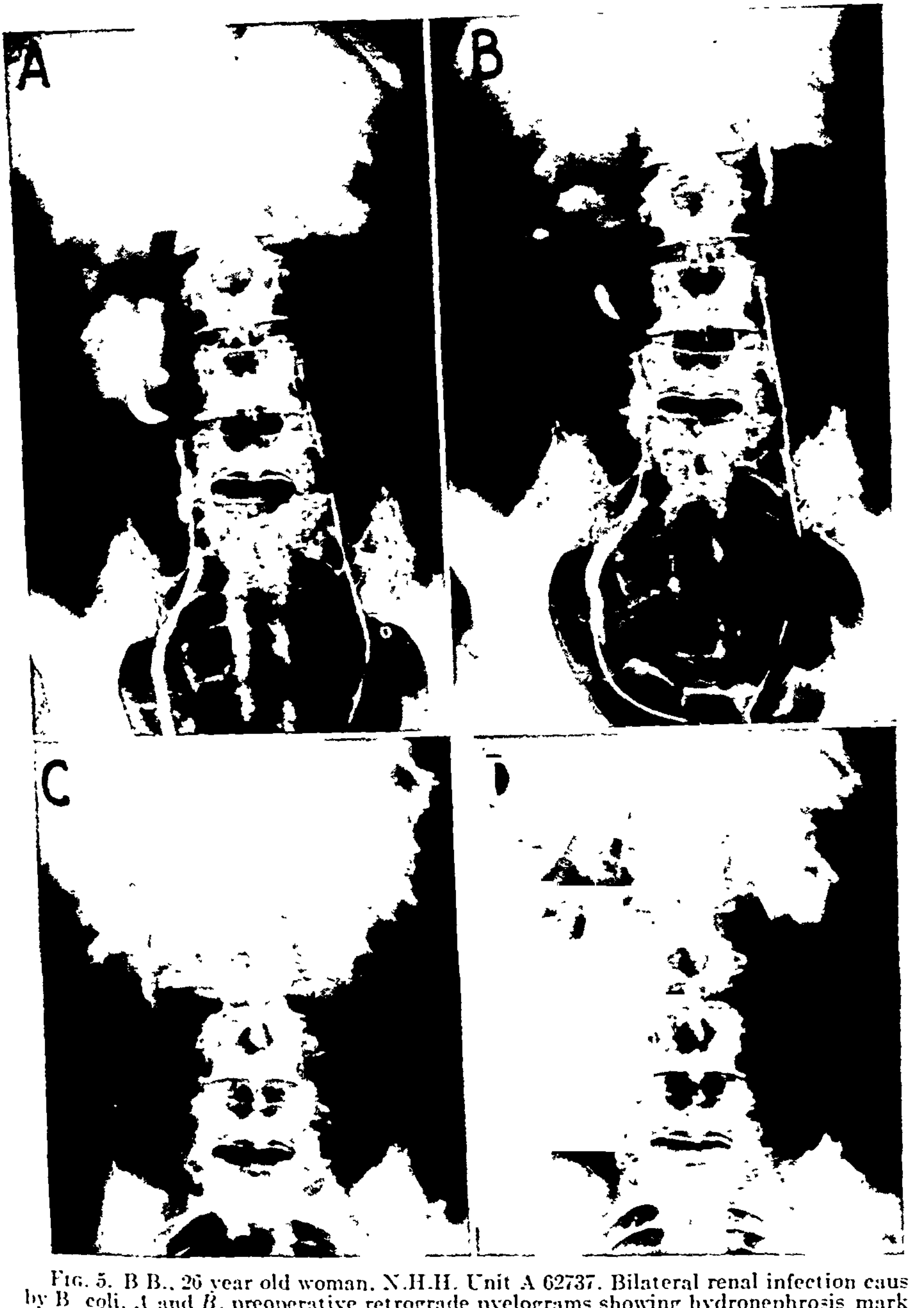

FIG. 5. B B., 26 year old woman. N.H.H. Unit A 62737. Bilateral renal infection caused by B coli. *A* and *B*, preoperative retrograde pyelograms showing hydronephrosis marked on right, moderate on left, caused on both sides by intrinsic stenosis of ureteropelvic junction Bilateral operations 6 weeks apart. *C*, excretory urogram 1 year after operation. *D*, excretory urogram 2 years after operation. Urine remains sterile. 2-hr. PSP excretion 59 per cent before operation, 73 per cent 2 years after operation.

We believe that the indications for this operation are in general those which lead one to decide on conservation rather than removal of the obstructed organ.

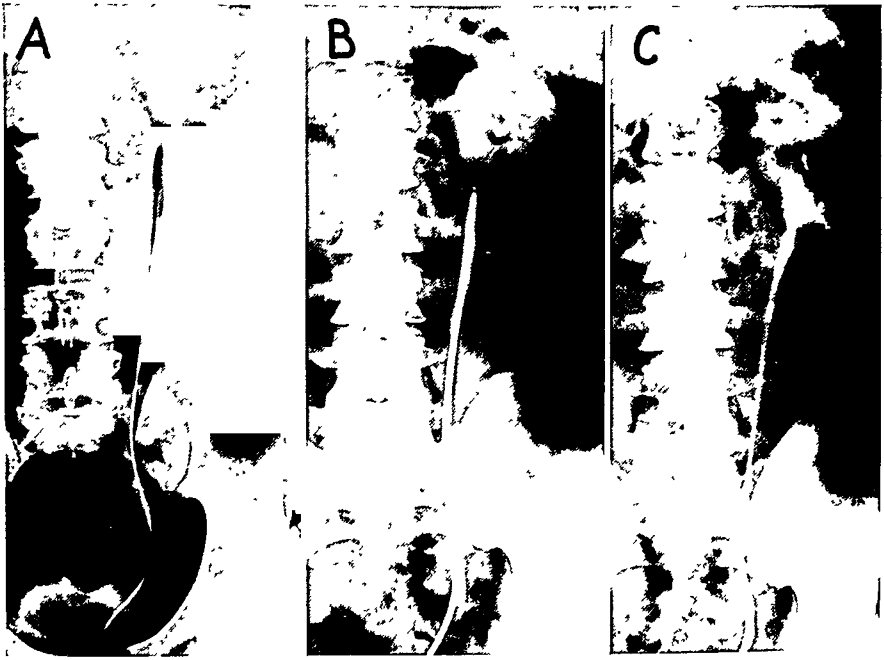

FIG. 6. P.H., 30 year old man, N.H.H. Unit B 47104. Right nephrectomy 3 years previously in another hospital after failure of attempted repair of right hydronephrosis with stones. *A*, retrograde pyelogram showing narrowing of upper left ureter caused by intrinsic stenosis. Operation refused at this time. *B*, retrograde pyelogram 5 months later during a seizure of pain in the left flank. Note resistance to injection of skiodan through upper ureter. *C*, retrograde pyelogram 15 months after operation. PSP 20 per cent in 15 minutes. Urine normal.

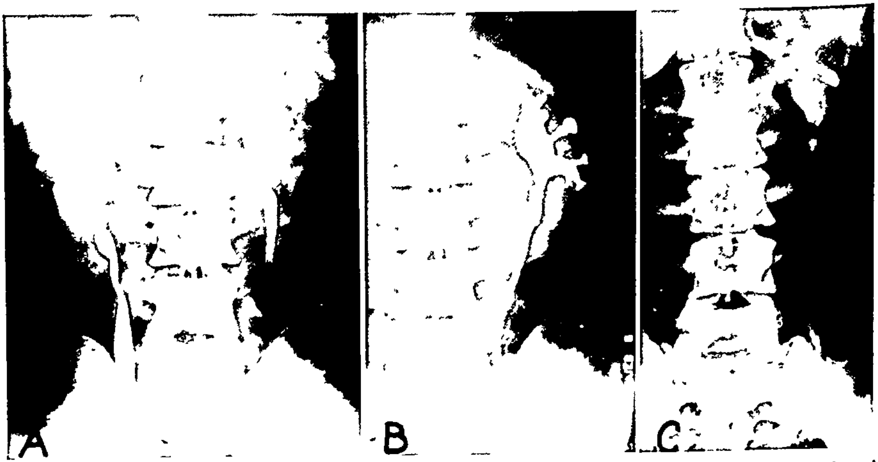

FIG. 7. L C., 17 year old boy, N.H.H. Unit B 85156. *A*, retrograde pyelogram showing giant hydronephrosis on right requiring nephrectomy. Moderate hydronephrosis on left caused by intrinsic stenosis of upper ureter *B*, retrograde pyelogram 4 months after operation. *C*, excretory urogram 2 years after operation. Urine normal. 2-hr. PSP excretion 45 per cent before operation, 55 per cent 2 years after operation.

The operation as we have described it is applicable to obstructions at or just below the ureteropelvic junction. There must, of course, be a reasonable prospect of recovery of function by the operated kidney.

The limitations of this operation are in general those which contraindicate conservative plastic surgery. The presence of compensatory hypertrophy in the opposite kidney probably precludes satisfactory restoration of function in the operated kidney. Our series does not test this maxim, since none of our cases had contralateral compensatory hypertrophy. The operation as described here is not applicable to long strictures of the upper ureter. A modification of it, using a pedicle graft of extrarenal pelvis to reach below the stricture, is feasible and should be tried. The presence of long standing pyelonephritis in the operated kidney seems to jeopardize the result. Certainly the contracted, pyelonephritic kidney offers no hope of satisfactory recovery of function. The age and general condition of the patient, the severity and duration of infection and the status of the opposite kidney are matters that defy generalization, but all are important in determining operability.

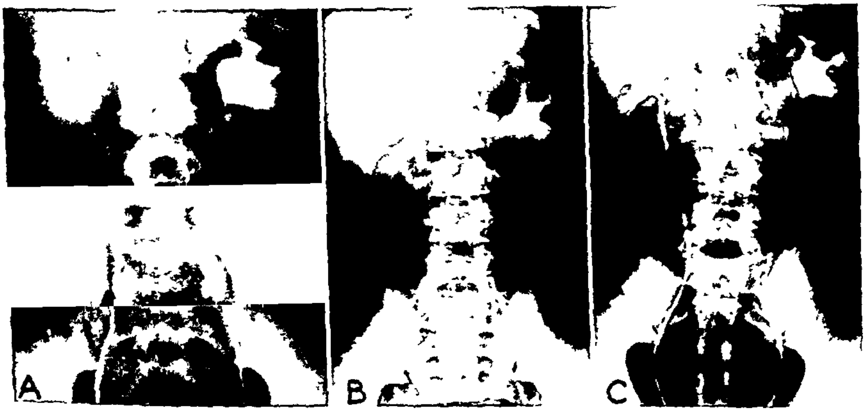

FIG. 8. G.B., 10 year old boy, N.H.H. Unit B 12117. *A*, retrograde pyelogram showing large hydronephrosis on right associated with a large aberrant artery and vein crossing ureteropelvic junction. Urine sterile. Right kidney repaired without urinary drain or splint. *B*, excretory urogram 2½ years after operation *C*, retrograde pyelogram 7½ years after operation. Urine remains normal. Now excretes 20 per cent PSP from right kidney and 20 per cent from left in 15 minutes.

It is interesting to point out that 6 of these 30 cases were closed at operation without using the T-tube or any other urinary drain or splint. These patients did not have infection before operation. One is mentioned above as having had a subsequent nephrectomy, probably because of premature instrumentation after operation. The other 5 healed nicely and have good results. The chief virtue of this modification is that one avoids the infection which is inevitable when a tube or splint is inserted in the kidney or ureter. Thus the patient goes through the entire operative experience without being exposed to renal infection, certainly an ideal we would like to realize in all urinary tract surgery. We are not yet prepared to propose this as a regular procedure, but our results are encouraging, and they serve at least to indicate the fundamental soundness of this type of anastomosis.

We would like to emphasize the advantages of the ureteral T-tube when drainage and splinting are desired. The upper arm of the tube splints the anastomosis adequately and prevents pooling of the urine in the pelvis. Urine is carried down the ureter or out to the drainage bottle, depending on variations in the hydrodynamics within the ureter or the drainage system. Usually the largest portion of the output from the operated kidney is collected in the drainage bottle. The infected renal scar which results from nephrostomy is avoided. The kidney itself is not injured. Prompt healing of the ureter without stricture is proved by the postoperative follow-up. The position of the drainage site below the anastomosis rather than above it precludes the development of troublesome fistula.

See figures 2 to 8.

CONCLUSIONS

In 30 cases we have used an operation involving resection of the pelvis and ureteropelvic junction and anastomosis of the ureter to the most dependent portion of the remaining pelvis. There have been three failures described above. Twenty-seven patients have had good anatomical, functional and symptomatic results. The ureteral T-tube is an effective drain and splint and does less damage than other appliances used for the same purpose. In those patients followed from 5 to 7 years the renal function has been maintained, and the roentgenograms show no tendency for late constriction at the site of anastomosis. The value of the operative procedure described is the permanency of the anatomical and physiological results.

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REFERENCES

Davis, D. M.: Intubated ureterotomy. Surg., Gynec. & Obst., **76:** 513, 1943.

Deming, C. L.: Ureteropelvic obstruction due to extrinsic and intrinsic lesions of the ureter as a clinical entity and its treatment. J. Urol., **50:** 420, 1943.

Foley, F. E. B.: New plastic operation for stricture at the ureteropelvic junction. J. Urol., **38:** 643, 1937.

Gibson, T. E.: Hydronephrosis; classification and repair of ureteropelvic obstructions. Surg., Gynec. & Obst., **80:** 485, 1945.

Henline, R. B. and Hawes, C. J.: Ureteropelvic obstructions: Symptoms and treatment. J.A.M.A., **137:** 777, 1948.

McIver, R. B.: Plastic surgery of the renal pelvis. J. Urol., **42:** 1069, 1939.

O'Conor, V. J.: Value of nephrolysis, ureterolysis and nephropexy in selected patients. J.A.M.A., **93:** 1114, 1929.

Quinby, W. C.: Factors influencing the operative procedure in hydronephrosis. J.A.M.A., **93:** 673, 1929.

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INTUBATED URETEROTOMY

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About 7 years ago I made my first contribution on the subject of intubated ureterotomy.[1] A further report was made to this Association at its meeting in Buffalo in 1947 in collaboration with Drs. G. H. Strong and Dr. Willard Drake.[2] In these articles I expressed the opinion that this operation would prove to be the most practical and the most successful procedure for all intrinsic ureteropelvic and upper ureteral narrowings. Since that time experience has in my own case strengthened this opinion, and I have heard many reports of successful operations performed by others. The points of superiority are: first, the operation is equally applicable to all cases, regardless of the length, location or multiplicity of the strictures; second, it is simple and rapid of performance; third, no sutures whatever are used, so that no dependence need be put on the holding of sutures; and fourth, since the splinting tube can be left in place as long as desired, good results have been obtained in many cases even in the presence of gross infection.

Some surgeons have had difficulties and failures, including ourselves. I believe that in each instance the difficulties have been due to errors in technique, and we have attempted to remove the causes of the imperfect results by modifying the method of performing the operation.

1) Adequate drainage of the kidney pelvis must be supplied during the time the splinting tube is in place. It became apparent early in our experience that the stem of a T-tube was not adequate for this purpose, and a separate pelvic drainage tube was inserted at each operation. This made the stem of the T-tube superfluous, so that the use of T-tubes was discontinued, and straight smooth rubber tubes used instead.

2) Drainage tubes emerging through a pyelotomy incision functioned better and were subject to fewer complications than those emerging through a nephrotomy incision. The pyelotomy incision is therefore now used in all cases except those where, owing to an intrarenal pelvis, there is insufficient room for a pyelotomy incision.

3) In several cases secondary strictures developed at the point at which the lower end of the splinting tube had rested in the ureter. Efforts were therefore made to use longer splinting tubes, and bring their lower ends as far down in the ureter as possible. These efforts culminated in the development of a stainless steel intubating bulb (fig. 1). To use this bulb, a panendoscope is passed just before the operation, and the lower ureter calibrated with bulbs to make sure that the intubating bulb of the size selected will pass through it. If necessary ureteral meatotomy may be carried out at this time. A Walther dilator

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Read at annual meeting, American Urological Association, Washington, D. C., June 1, 1950.

[1] Surg., Gynec. & Obst., 76: 513–523, 1943.

[2] J. Urol., 59: 851–859, 1948.

shaft armed with a short filiform tip is then passed up the ureter to the narrowed area, and left in place. When the ureter is opened, the upper end of the shaft is recovered, the filiform tip removed, and the intubating bulb screwed on. The splinting tube fits tightly into the bulb, and is held there by a stout silk thread passing through a hole in the central post. Traction on the shaft by an assistant then pulls the splinting tube through the entire length of the ureter, the bladder and the urethra. A long tube is necessary, and we often employ a Levine duodenal tube. The presence of this tube in the urethra makes voiding difficult, so that a No. 16 Foley balloon catheter is usually inserted into the bladder alongside it. With this arrangement patients are perfectly comfortable for as much as 4 or 5 weeks, and are able to be up and walk about freely. This technique has done away with secondary strictures.

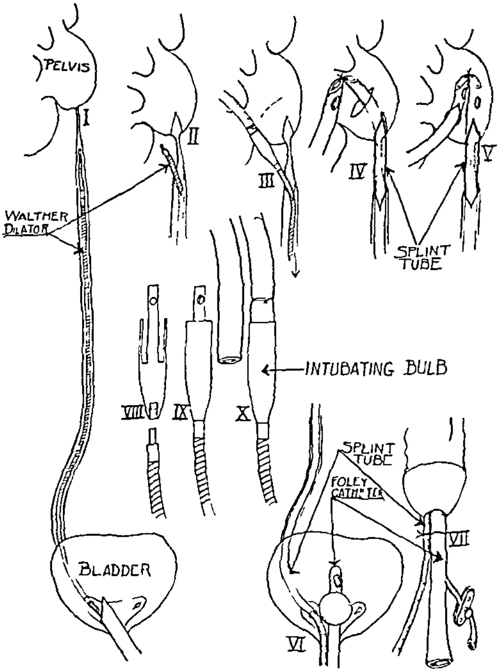

FIG. 1. Method of intubating entire ureter: *I*, Shaft of Walther dilator armed with short filiform tip and passed up ureter. *II*, Walther shaft recovered through ureterotomy and filiform tip removed. *III*, Intubating bulb with splint attached screwed to Walther shaft. *IV*, splint tube pulled through entire ureter and urethra; *V*, splint tube arranged in pelvis and attached to pyelostomy tube (it is better anchored as in fig. 2., *II* or *IV*). *VI*, No. 16 Foley catheter 5 cc bag in bladder. *VII*, Splint tube tied to Foley catheter. *VIII*, Construction of intubating bulb. *IX*, External view of bulb. *X*, Bulb with splint tube attached.

4) The deposition of calcareous sand in the splinting and drainage tubes is a serious matter, and may ruin an otherwise successful operation. Sanding of the tubes can be detected early by rolling them between the fingers near the points where they emerge from the body. The sand can be removed and further formation prevented by continuous drip irrigation with a buffered acid solution such

as Suby's solution or solution G. It is therefore necessary to see to it at the time of operation that the drains and tubes are so arranged that such irrigation can be carried out. Recently flexible, transparent tubing of a polyvinyl resin has been obtained, but too recently to report on its use. This material has a non-wettable surface, and it is said that no calcareous deposits can occur on it. If this proves to be the case, this new tubing will provide a valuable improvement.

5) Otherwise good results can be spoiled by angulation due to displacement of the ureter by the pull of badly placed tubes. It is necessary to assure that the ureter, with its contained splinting tube, follows a normal, straight course. It is therefore better to have the splinting tube terminate in the renal pelvis, rather than try to bring it to the surface through a nephrostomy or pyelostomy opening. If this is done the tube is thrown into a curve, and may displace the ureter. If the splinting tube traverses the entire ureter, it is easy to have it end in the pelvis.

6) The incised ureter, if in contact with the kidney, peritoneum, psoas or quadratus lumborum muscle, or any other organ, will adhere to it and lose its normal mobility. The normal ureter floats in the retroperitoneal and perirenal fat. It is therefore very important to see, at the end of the operation, that the pelvis and all of the exposed ureter are thoroughly surrounded by as thick a layer of fat as possible, to prevent such adhesions.

7) In arranging the splinting tube and drain, it is desirable to be able, at the end of the splinting period, to remove the splinting tube while the kidney drainage tube is still in place. There are three reasons for this: 1) skiodan solution can immediately be injected through the drainage tube and a film taken showing the contour of the pelvis and ureter, and whether the solution flows easily to the bladder; 2) the drainage tube may be clamped for a day or two to make sure that the ureter functions normally; and 3) if there is any doubt about proper ureteral function, especially in the case of a solitary kidney, drainage can be restored instantly at any time by unclamping the tube. Consequently, certain tube arrangements formerly used have now been abandoned.

The considerations mentioned rule out a number of tube arrangements which have become well known. The Cummings tube requires nephrostomy, the ureteral part is apt to be too small, and the setup is not very favorable for acid irrigations. The various T-tube arrangements are unsatisfactory for the reasons noted. We now try in every case to have the splinting tube follow a straight course, to have it terminate in the pelvis, and to keep it independent of the pelvic drainage tube, so that the two tubes need not be removed at the same time. It was found possible to retain the splinting tube in place by anyone of three methods and still be able to remove it independently. These methods are, first, to stiffen the splinting tube with a whalebone or nylon stylet; second, to pass a silk thread, fastened to the end of the splinting tube, out through the pelvic wall and through the abdominal parietes, where it can be tied over a bit of rubber tubing or gauze until the time arrives for the removal of the tube; and, third, a similar silk thread can be brought out through the lumen of the pelvic drainage tube, and fastened exteriorly for as long a period as necessary (fig. 2). The use of a silk thread was first suggested by Dr. F. E. B. Foley.[3] All of these methods are satisfactory, and permit acid irrigations in either direction,

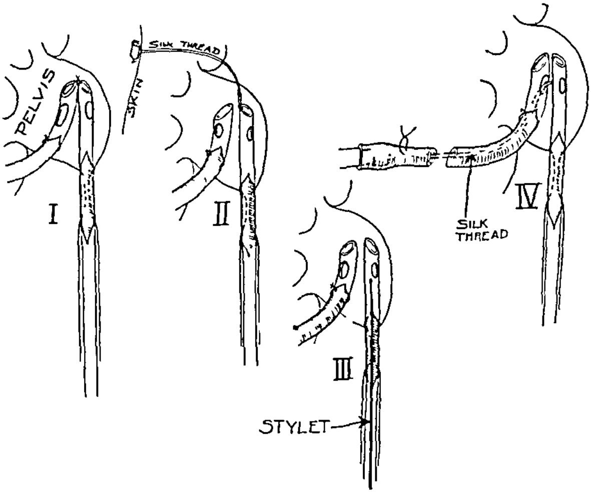

FIG. 2. Various methods of anchoring ureteral splinting tube. *I*, Splint tube sutured to pyelostomy tube with silk thread. When pyelostomy tube is withdrawn, splint tube follows it out. *II*, Splint tube anchored with silk thread passing out through pelvic wall and abdominal parietes. When splint tube is withdrawn through urethra, silk thread is cut and buried part follows splint tube out; *IV*, Splint tube anchored by silk thread passing through lumen of pyelostomy tube; *III*, Splint tube (which extends through entire ureter and urethra) stiffened by whalebone or nylon stylet so that it will not be expelled.

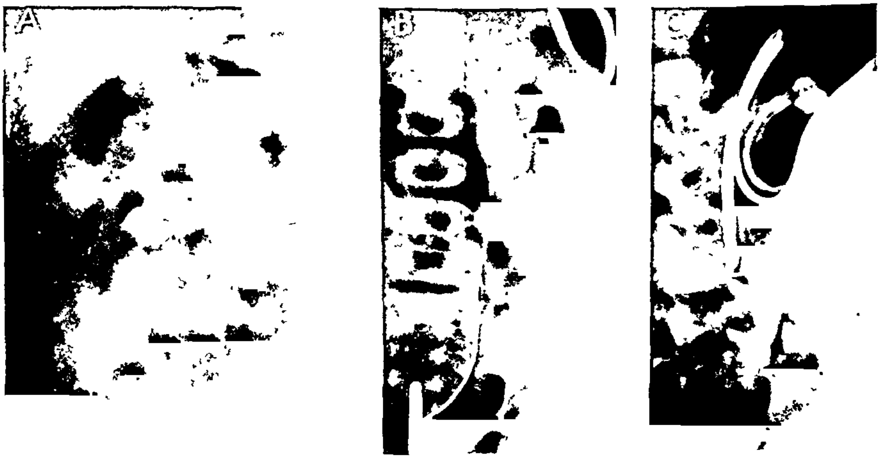

FIG. 3. E. H., female, aged 18 months. Left panel, excretory urogram showing large left hydronephrosis and huge right hydronephrosis. No symptoms, urine clear, palpable mass in right upper quadrant. Middle panel, retrograde pyelo-ureterogram, showing two areas of narrowing, in intramural ureter and at ureteropelvic junction. Right panel, after first operation (intubated ureterotomy at ureteropelvic junction) showing large splint tube in upper ureter (size 12) and pelvic drainage tube.

but they all depend upon the intubation of the entire length of the ureter, so that the splinting tube can be removed from below.

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[3] Personal communication.

8) In cases where the ureter assumes a spiral or pigtail curl just below the ureteropelvic junction, it has been found that this is due to the fact that one side of the ureter is longer than the other. Simple splitting and intubation does not correct this condition, and the spiral curl may reappear after an otherwise

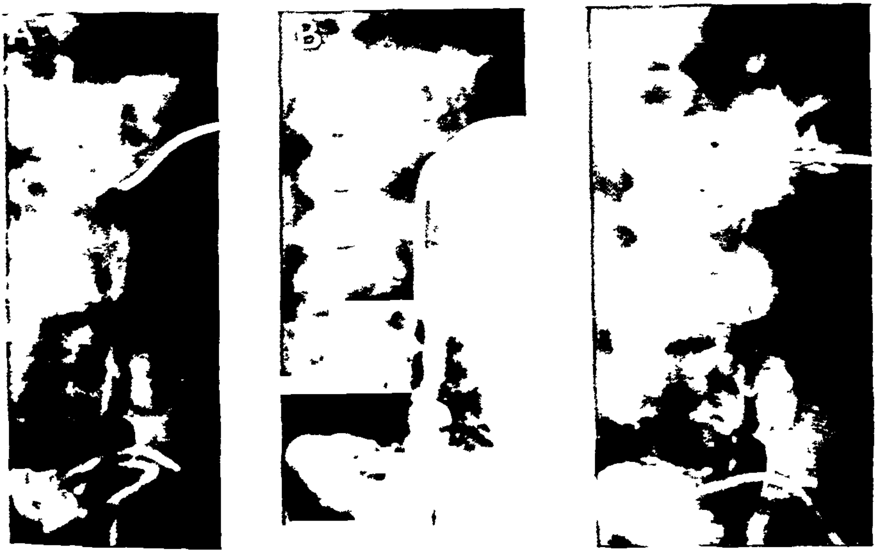

FIG. 4. E. H., same as figure 3. Left panel, after second operation. Large splint tube (size 12) in lower ureter, emerging through cystotomy incision. Middle panel, lower ureter outlined with skiodan after withdrawal of splint tube. Right panel, skiodan solution injected through pelvic drainage tube is rapidly conducted to bladder.

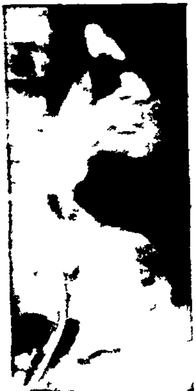

FIG. 5. E. H., same as figure 3 Retrograde pyelo-ureterogram made 4 months after second operation. Ureter now admits No 10 bulb with ease. Urine sterile.

successful operation. This difficulty can be met by removing one-half or more of the circumference of the ureter over a sufficient distance, selecting either the short side or the long side. I believe that the short side is preferable. The ureter is then permitted to reform about a splint tube. Another solution would be resection and reimplantation.

9) If any sutures are used to hold the strip of incised ureter against the splinting tube, great care must be taken to tie them loosely, so that they cannot cut off the blood supply of the ureter. I know of 2 cases of complete obliteration of the ureter, almost certainly caused by tying such sutures too tightly.

It sometimes happens, particularly in young children, that it is impracticable to intubate the entire length of the ureter. If this is the case, it is necessary to bring the upper end of the splinting tube out through an upper pole nephrotomy or through a pyelotomy incision made as high in the pelvis as possible. If this is done every effort must be made to keep the course of the ureter straight and normal by suturing pads of fat about it.

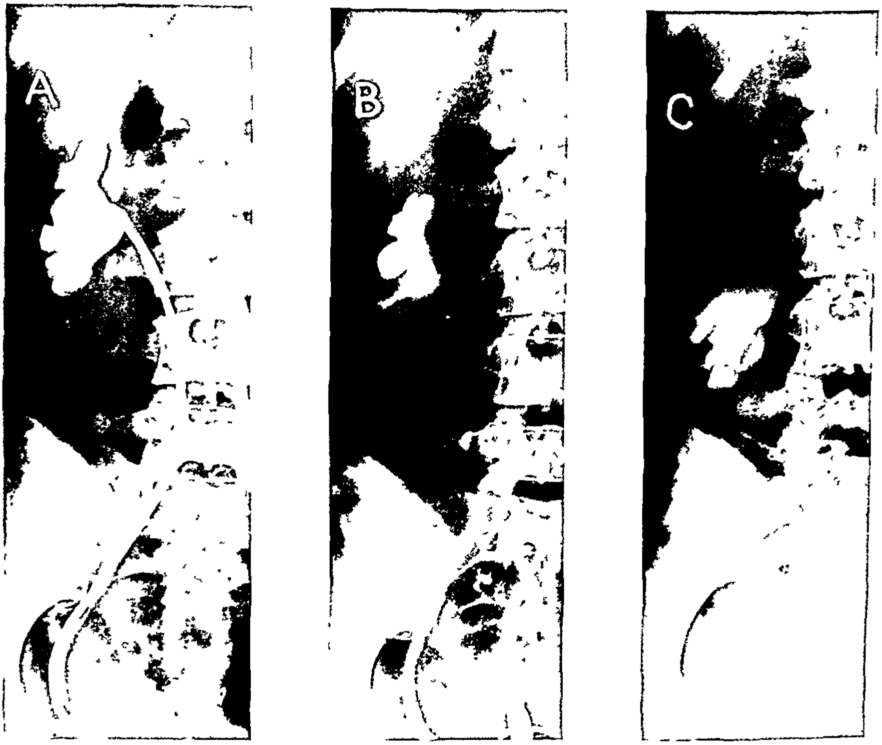

Fig. 6 D. B., woman, aged 26. Anorexia, nausea and vomiting for 4 years, leading to emaciation (weight 92 pounds). Generalized abdominal pain, more on right side. Right panel, right retrograde pyelogram, moderate hydronephrosis. Middle panel, right retrograde pyelo-ureterogram, showing 180 degree curve in upper ureter Right panel, erect emptying film taken 10 minutes after removing catheter showing marked retention in pelvis.

It is true that one is never sure just what conditions may be met, so that one must be ready at any time to improvise new tube arrangements, always keeping the previously stated fundamental principles in mind.

Intubated ureterotomy has been used in patients as old as 72 years, and as young as 18 months. Results are satisfactory in about 90 per cent of all cases. See figures 3, 4, and 5. Subsequent nephrectomy has had to be performed in only one of my personal cases. Most of the poor results are now known to have been due either to faulty technique or to the leaving of a fragment of stone in

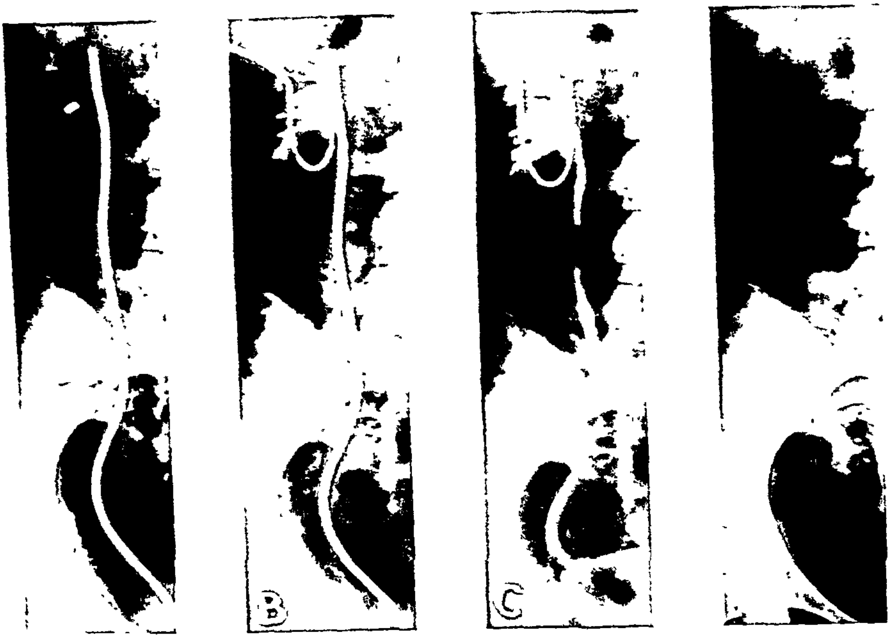

Fig. 7. D. B., same as figure 6. Left panel, film taken 4 weeks after operation (intubated ureterotomy) showing entire ureter intubated. Left middle panel, pelvis filled with skiodan, showing hydronephrosis already reduced. Right middle panel, ureter filled with skiodan just after withdrawal of splint tube, showing normal outline. Right panel, erect emptying film taken 10 minutes after withdrawal of splint tube (pelvic tube clamped) showing complete emptying of pelvis. One year after operation, patient has gained 35 pounds and is in perfect health. Urine sterile.

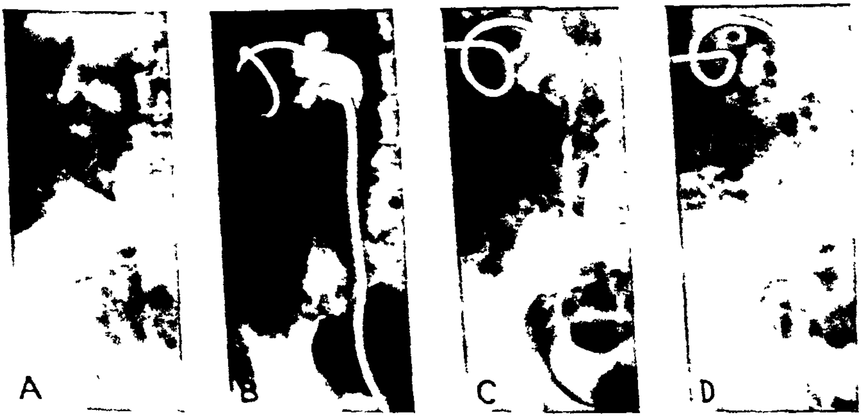

Fig. 8. S. M., woman, aged 48. Pain in right upper quadrant and back. Left panel, erect emptying film taken 10 minutes after withdrawing catheter, showing retention in pelvis. Three calculi in middle calyceal system. Left middle panel, after operation (intubated ureterotomy and nephrolithotomy, two nephrotomy incisions necessary). Entire ureter intubated. Right middle panel, ureter filled with skiodan after withdrawal of splint tube showing normal outline. Right panel, erect emptying film taken 10 minutes after withdrawal of splint tube (pelvic tube clamped) showing complete emptying of pelvis and ureter. Six months after operation, patient is well, urine sterile.

the pelvis. In one case with large bilateral hydronephrosis, infection and stone formation have continued, in spite of the fact that both ureters now admit a

No. 14 bulb with ease. It should be noted that small hydronephroses sometimes cause very severe symptoms. In case of doubt, the pelvis must be filled with an opaque medium, and an emptying film taken in minutes, the patient meanwhile standing erect. In one case so detected a small hydronephrosis caused severe pain, nausea, vomiting, anorexia, and emaciation, all completely relieved after relief of the obstruction by intubated ureterotomy. See figs. 6, 7, and 8.

One of the first 5 cases operated on *about 8 years ago has been lost sight of,* but was in good health when last heard from. The other 4 are known to be well, and 2 of them have remained under close observation. One has had 2 subsequent pregnancies, one ectopic and one normal, without the slightest urinary complication. The other is in perfect health, with no symptoms, sterile urine, normal renal functional tests, and a ureter which admits a No. 14 bulb with ease. The renal pelvis has returned to normal.[4]

I believe that this operation has now proved its merit, and that the results to be obtained with it are such that it should be in the repertoire of every urologic surgeon. It is not my intention to make any further publication on the general subject of this operation, but only on its refinements and experimental bases, and I offer it to the urological profession with every confidence that intubated ureterotomy will be found to be an extremely valuable procedure.

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[4] J. Urol., **57**: 233–237, 1947; **59**: 851–859, 1948.

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THE EFFICACY OF PLASTIC URETERAL AND URETHRAL CATHETERS FOR CONSTANT DRAINAGE

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It is the purpose of this communication to describe the characteristics of certain plastic catheters, especially polyethylene, and to illustrate definite advantages these catheters have in selected problems encountered in urologic surgery. A comparison with common ureteral catheters will be made on the basis of our experience during the last 2 years. Although methyl methacrylate (lucite) and nylon have been found to be well tolerated by tissues,[1] neither of these plastics has been ideal for the making of catheters. The woven nylon ureteral catheter has been quite satisfactory for routine use but leaves much to be desired in certain instances especially when prolonged ureteral drainage is necessary. None of the plastics available to date are ideally suited for the production of a "perfect" catheter; however, polyethylene, as will be demonstrated, has many properties which make it ideal for use in special circumstances. Polyvinyl acetate has been used to a more limited extent and the results indicate the need for further study of this material. The initiation of and an added impetus to the application of plastics to surgery has been gained from the work of Meyers,[2] Ingraham, Alexander and Matson,[3, 4] Hufnagel,[5] Ferris,[6] Davalos,[7] de Nicola[8] and Matson.[9]

CHEMICAL AND PHYSICAL PROPERTIES OF POLYETHYLENE*

Polyethylene is a polymer of ethylene with each molecule containing 200–1,000 or more ethylene units and having a molecular weight of about 18,000. It is a tasteless, odorless, translucent thermoplastic resin with a specific gravity of 0.92.[3]

Its thermoplastic point is 110–115C, therefore it can be sterilized by boiling if done with care, but it tends to maintain the shape that it is boiled in. It is

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Read at annual meeting, American Urological Association, Washington, D. C., June 1, 1950.

[1] Ingraham, F. D., Alexander, E., Jr. and Matson, D. D.: Synthetic plastic materials in surgery. N. Eng. J. Med., **236**: 362-368; 402-407, 1947.

[2] Meyers, L.: Intravenous catheterization. Am. J. Nurs., **45**: 930-931, 1945.

[3] Ingraham, F. D., Alexander, E., Jr. and Matson, D. D.: Polyethylene, a new synthetic plastic for use in surgery. J. A. M. A., **135**: 82-87, 1947.

[4] Ingraham, F. D., Alexander, E., Jr. and Matson, D. D.: The use of synthetic plastic materials in surgery. The Practitioner. **162**: 152-159, 1949.

[5] Hufnagel, C. A.: Permanent intubation of the thoracic aorta. Arch. Surg., **54**: 382, 1947.

[6] Ferris, D. D. and Grindley, J. H.: Use of polythene and polyvinyl tubing in ureterostomy, nephrostomy and cystostomy. Proc. Mayo Clin., **23**: 385, 1948.

[7] Davalos, A.: Experimental use of polyethylene tubing in the urethra. Scientific exhibit, 44th annual meeting. American Urological Association, May 1949, Los Angeles.

[8] de Nicola, R. R.: Artificial urethra. J. Urol., **63**: 168-172, 1950.

[9] Matson, D. D.: A new operation for the treatment of communicating hydrocephalus. Report of a case secondary to generalized meningitis. J. Neurosurg., **6**: 238-247, 1949.

* The polyethylene tubing used in this work was supplied by the Suprenant Manufacturing Company of Boston and converted into catheters by one of the authors (H. P. B.).

flexible and pliable, yet strong and resilient. Its chemical and physical properties make it adaptable commercially for the extrusion of tubing of varying sizes. In the pure state it is quite inert and therefore there is minimal tissue reaction to it. Its water repellent or nonwetting properties are similar to those of paraffin which it resembles in appearance. Since the water repellent and nonclotting properties are directly proportional, it is obvious that blood coagulation is markedly delayed in polyethylene tubing as has been demonstrated by Donovan and Zimmermann.[10] This plastic is nonopaque to the x-ray; it will be shown later that this disadvantage is easily circumvented.

COMPARISON OF POLYETHYLENE CATHETER WITH ORDINARY URETERAL CATHETER

At the outset we wish to emphasize that it is not being suggested that polyethylene catheters be used to replace the ordinary ureteral catheter but rather to supplement the latter in certain instances. The interior surface of the woven ureteral catheter in common use today is shown in figure 1, *A*. The extreme irregularity and the multiple interstices stand out in sharp contrast to the smooth inner surface of the polyethylene catheter exhibited in figure 1, *B*. It is obvious that the surface of the former would predispose to deposition of the constituents of urine and blood coming in contact with it. The smooth surface of polyethylene facilitates mechanical cleansing and therefore sterilization by soaking can be accomplished with greater confidence. Prolonged soaking in no way affects polyethylene as it is impervious to acids, alkalies, alcohol, ether and acetone. A comparison of size for size of the two types of catheter (fig. 1, *C*) shows

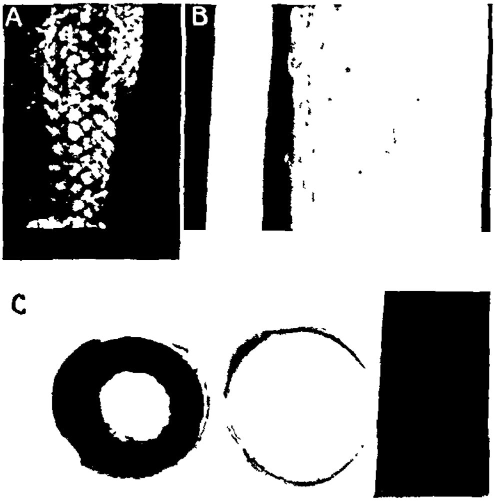

FIG. 1. *A*, illustrates irregular inner surface of a 5F woven ureteral catheter. Interwoven fibers and multiple interstices can be easily seen. *B*, illustrates smooth, waxy inner surface of a 5F polyethylene ureteral catheter. *C*, illustrates cross sections of comparable woven (left) and polyethylene (right) ureteral catheters respectively of same outside diameters. Larger lumen of polyethylene catheter is clearly demonstrable on reader's right.

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[10] Donovan, T. J. and Zimmerman, B.: The effect of artificial surfaces on blood coagulability with especial reference to polyethylene. J. of Hemat., 4: 1310–1316, 1949.

that the polyethylene has a larger lumen. This fact is further demonstrated by a comparative table of inside and outside diameters (table 1). In most cases the actual lumen area is twice as great in the polyethylene catheter. The nonclotting properties[10] as well as the larger lumen decrease the tendency for obstruction by blood clot, exudate, and urinary salts. It is our impression, however, that over a period of weeks the deposition of exudate and urinary salts may occasionally occur in or on the polyethylene catheter.

Owing to the inert nature of pure polyethylene there is a minimal tissue reaction.[2] The implications of this property are obvious. In no case in our experience has a polyethylene catheter been expelled from the ureter. This is a distinct advantage and in contrast to the general experience with inlying woven ureteral catheters. This fact is attributable to the inertness, malleability and resiliency of polyethylene which allows the catheter to conform to the course of the ureter without significantly altering ureteral dynamics.

TABLE 1. *Comparison of lumen of woven and polyethylene ureteral catheters of same circumference*

OUTSIDE CIRCUMFERENCE FRENCH SCALE	INSIDE CIRCUMFERENCE FRENCH SCALE	
	Woven	Polyethylene
mm	mm	
5	2.5	3.5
6	3	4
7	3	4.5
8	4	5.5
9	4.5	6
10	5	7
12	5.5	10

It is also believed that the resiliency of the polyethylene catheter renders it less likely to damage the ureter in the process of passing it up an obstructed ureter. In only 1 case have we been unable to pass a polyethylene catheter when a woven ureteral catheter could be passed.

The cost of polyethylene catheters is much less than that of ordinary ureteral catheters since the material is extruded in mass quantities rather than being woven as a tube and covered with a lacquer or varnish. Finally, both during use and storage the polyethylene catheter maintains its innate physical properties consistently for a longer period of time.

CLINICAL APPLICATION OF POLYETHYLENE CATHETERS TO PROLONGED URETERAL DRAINAGE

The characteristics of polyethylene tubing previously described make it adaptable to use in a variety of conditions of the mid and upper urinary tract. The larger smooth lumen, resiliency, malleability, nonwetting property and increased tissue tolerance of these catheters make them effective in the management of the following conditions:

1. *Bleeding into the renal pelvis and obstruction by blood clot.* The diminished

tendency for blood to clot in these tubes allows for improved drainage and likewise for a more successful evacuation of organized clot from the pelvis. The striking improvement in 2 such cases is illustrated in figures 2 and 3. They may be employed similarly in selected cases of nonoperative traumatic injury of the kidney, when operation is being withheld, and in borderline cases of severe contusion or partial rupture of the kidney. Efficient drainage and evacuation of

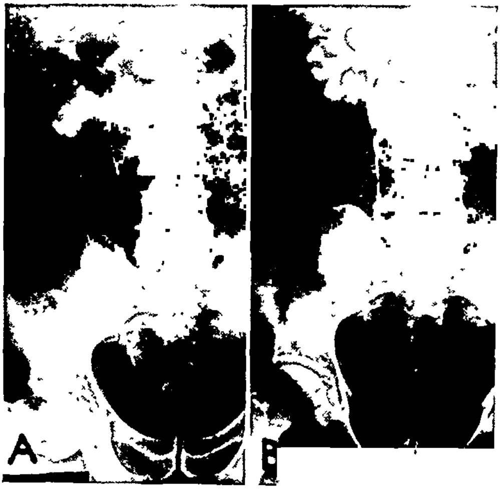


Fig. 2. J. A., a man aged 52, had multiple calculi in right kidney. Nephrolithotomy, right; nephrostomy. Ten days after operation, passage of blood and clots down right ureter as well as leakage of urine from flank. Polyethylene catheter 7F was passed. *A* shows irregularity of pelvis due to retained clot and extrarenal extravasation owing to failure of pelvis to heal caused by blood clot in pelvis and ureter. *B* shows retrograde pyelogram after 7 days of drainage with a polyethylene catheter. Pelvis is completely healed and free of blood clot.

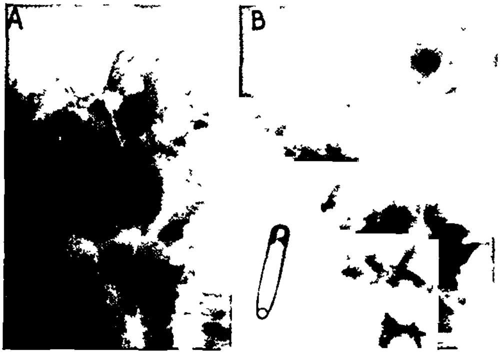


Fig. 3. G. T., a man aged 37, had right staghorn calculus, hypoplasia of left kidney and bilateral pyelonephritis. Nephrolithotomy, right; nephrostomy. Complication: Persistent fistula in flank and repeated passage of blood clot down ureter starting on eleventh postoperative day. With polyethylene catheter drainage of renal pelvis, bleeding ceased in 24 hours and drainage became clear except for aspiration of organized clot. *A*, retrograde pyelogram shows distortion of the pelvis by retained blood clot. *B*, retrograde pyelogram (4 cc) 7 days later when drainage was clear shows no evidence of remaining clot in renal pelvis. Urinary fistula in flank was healed 48 hours after polyethylene catheter drainage had been instituted.

clots accomplish decompression of the pelvis, diminished congestion and arrest of hemorrhage.

2. *Obstruction of ureter by infection or stone.* The increased tissue tolerance and diminished tendency to expulsion as well as the larger lumen of these catheters confer an advantage in such cases for prolonged effective drainage. Figure 4 illustrates the usage in such an instance.

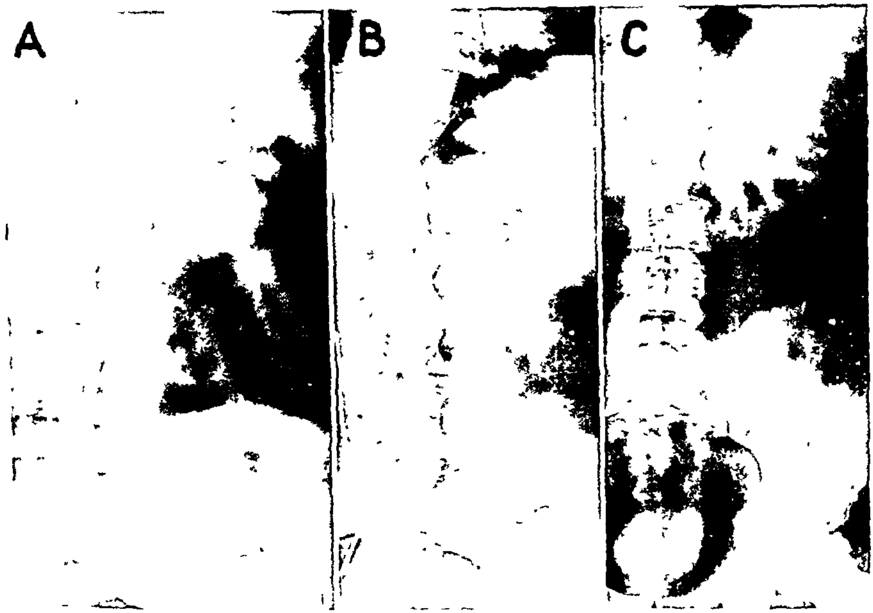


FIG. 4. R. H., man aged 42. Ureteral calculus obstructing left ureter; pyelonephritis left. Ureterolithotomy, left lower third Complication· Hydronephrosis, left, secondary to ureteritis, asymptomatic and discovered by excretory urography 3 weeks after ureterolithotomy. *A* shows dilatation of left renal pelvis and ureter at this time. *B* shows retrograde pyelogram (4 cc) after 7 days' drainage with a polyethylene catheter. Previous dilatation is notably absent. *C*, excretory urogram at 15 minutes 4 months later shows a normal pyelogram

3. *Preliminary drainage of infected hydronephrosis or pyonephrosis.* It seems that improved ureteral and renal drainage may be effectively accomplished in some patients in this category, at times obviating the necessity for a nephrostomy in seriously ill patients, as shown in figure 5. In this case inflammation and edema of the ureter improved during the presence of an inlying polyethylene catheter as evidenced by urine being passed around the catheter which was functioning satisfactorily. A striking decrease in the size of the kidney in this case was manifested by physical and roentgenographic signs.

4. *Renal calculi and sulfonamide crystalluria.* It is believed that more successful therapy directed toward dissolution of renal calculi by lavage may be accomplished by utilizing polyethylene catheters as the pathway of ingress and egress of solution M of Suby and Albright. Success has been experienced by many in the management of sulfonamide crystalluria with the ordinary ureteral catheter; some advantage may be gained in the more difficult cases with plastic catheters.

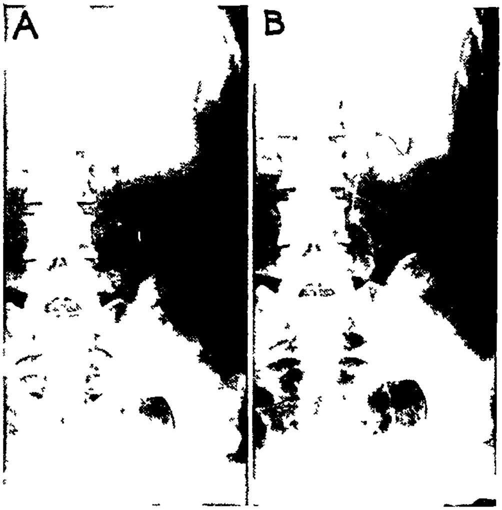


FIG. 5 K. W., woman aged 53 Diabetes mellitus; severe necrotizing pyelonephritis, left Postoperative nephrectomy, right, 4 months previously for pyonephrosis Complication· Anuria due to necrotizing pyelonephritis and ureteritis with obstruction of ureter by debris for 48 hours prior to admission. Left kidney was greatly enlarged, easily palpable and tender. *A* shows enlarged left renal shadow extending down almost to crest of ilium. *B*, retrograde pyelogram (4 cc) 2 weeks after polyethylene catheter drainage was instituted shows kidney definitely diminished in size and with loss of calyceal detail owing to necrotizing infection. Edema of ureter subsided enough while the catheter was in place to permit urine to pass around it into bladder to extent of several hundred cubic centimeters daily. Technique of drainage avoided necessity for nephrostomy in a moribund patient for 4 weeks at the end of which time she expired of renal insufficiency.

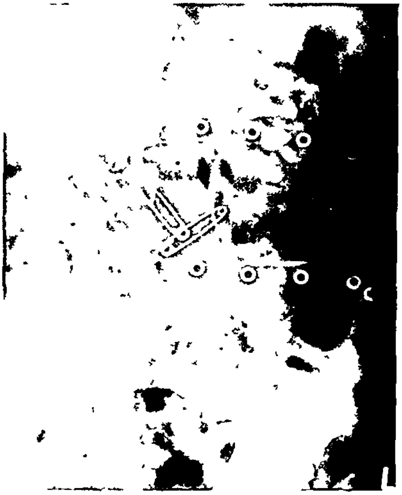


FIG. 6. F. W., man aged 55 Ureteral calculus, left; acute pyelonephritis and hydronephrosis, left. Ureterolithotomy, left Complication. Owing to severe degree of localized ureteritis and pyelonephritis polyethylene catheter drainage of the left renal pelvis was instituted through ureterostomy opening at time of operation. Retrograde pyelogram 12 days after operation with polyethylene catheter still in place. Some calyceal dilatation still present Prompt healing of ureter occurred upon removal of catheter and the patient continued to be well 2 months later without symptoms

5 *When postoperative drainage is needed.* a Ureterostomy, pyelostomy and nephrostomy: The nonclotting properties and excellent tolerance by tissues make polyethylene tubing desirable for these purposes. Figure 6 illustrates a very satisfactory result, obtained in the face of acute sepsis, of such usage. Figure 7 illustrates the use of a plastic catheter after ureteral meatotomy or after surgical excision of a portion of the bladder or electrocoagulation in proximity to the ureteral orifice. The use of such catheters for pyelostomy or nephrostomy is equally as applicable; this was first discussed and emphasized by Ferris and Grindlay [6]

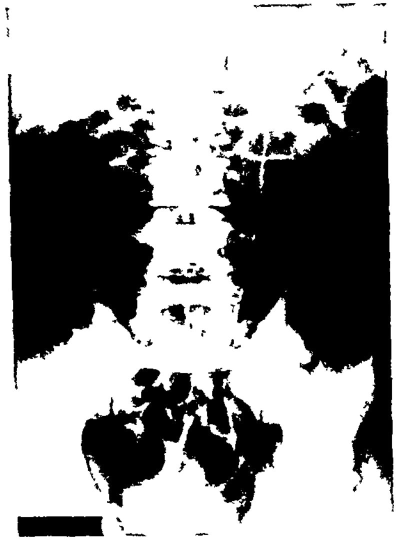
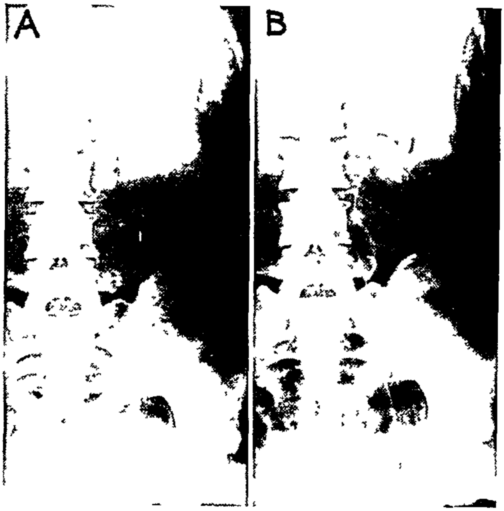


FIG. 7 E B., man aged 28 Ureteral calculus left. Ureteral meatotomy (cystoscopic). Complication Hemorrhage from ureterovesical junction. Cystotomy, removal of calculus and electrocoagulation of bleeder was carried out. Meatotomy was splinted for 7 days with No 8 polyethylene catheter with good toleration and good result. Retrograde pyelogram shows catheter in place and a normal renal pelvis 1 week later. This technique has been found to be useful after removal or electrocoagulation of papillomas in or about ureteric orifices.

b Pyeloplasty, ureteroplasty and urethroplasty: Some controversy exists in regard to the use of splints in plastic surgery of the urinary tract. When the operator desires and feels the necessity for using a splint that also serves as an effective drain, he may wisely choose a plastic material to accomplish his purpose. Figure 8 illustrates the result obtained in the treatment of a traumatic stricture of the urethra in a young boy. Pursuant to this experience the conservative management of filiform caliber strictures causing acute urinary retention has been successfully expedited in a number of cases. In these surgical intervention has been avoided or delayed until the patient's condition was improved.

Polyvinyl acetate has also been found to be quite satisfactory for urethral drainage following prostatectomy and repair of urethral stricture. However for long term drainage the material available to us showed a greater susceptibility to deposition of calcareous salts and exudate than did polyethylene. We believe



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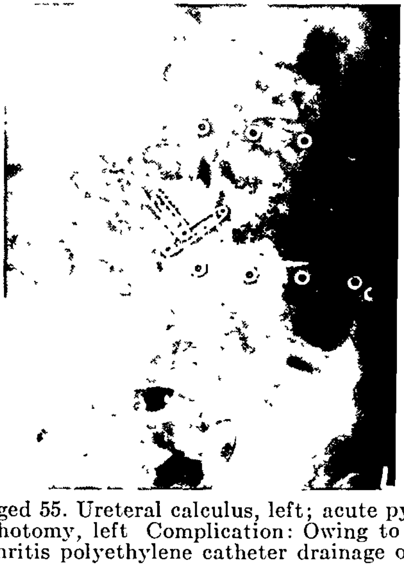

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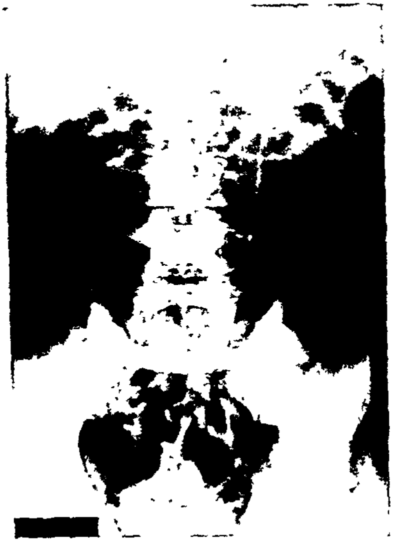

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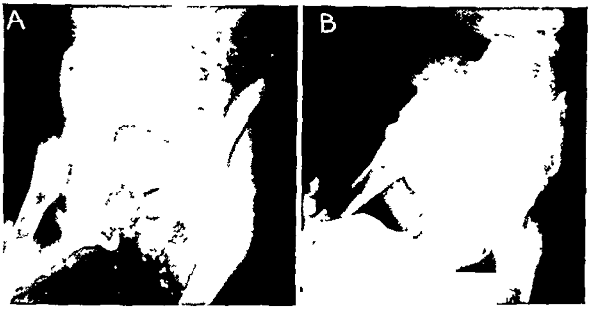

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TECHNICAL SUGGESTIONS TO AID IN THE USE OF PLASTIC CATHETERS

On the basis of our experience with plastic catheters during the last two years it is anticipated that the following suggestions may be helfpul to others using them. No marking or radio-opaque medium should be placed on the outside of the catheter as this destroys the inertness of the polyethylene. If a graduated woven catheter is passed inside the polyethylene catheter, the markings can be distinctly seen through the transparent plastic and the distance passed up the ureter accurately measured. A 3.5F woven catheter can be used in the smaller sizes and a 4F or 5F for the larger. With the woven catheter inside, the lumen of the polyetheylene catheter becomes radio-opaque. In addition the inside catheter aids in the passage up the ureter by rendering the polyethylene less flexible.

The experience of being unable to pass a polyethylene catheter beyond an obstruction in the ureter has been met and this difficulty solved by inserting a lubricated woven catheter into its lumen during the catheterization. The inner catheter is then easily removed without disturbing the position of the outer polyethylene tube.

Sterilization is best achieved by 1) rinsing with phisoderm or another effective detergent; 2) flushing with saline; 3) soaking in 1:500 zephiran, 1:1000 urolocide or their equivalent for 12–18 hours; or 4) they may be safely formalinized after thorough cleansing by 1 or 2.

The location of the catheter can be checked from time to time by injecting a small amount of radio-opaque medium into the catheter and simultaneously making a roentgenogram as shown in figures 2, 3, 5, 6 and 7.

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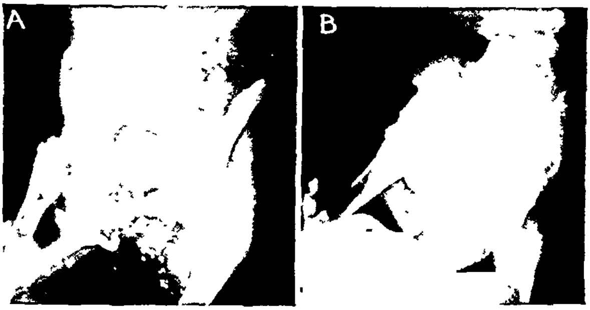

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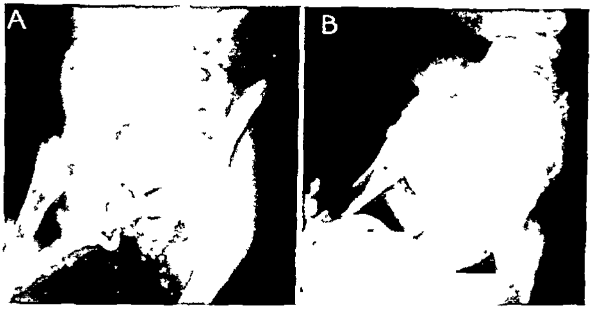

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DISCUSSION

DR. FREDERIC E. B. FOLEY (St. Paul, Minn.): This symposium has been for me the most engaging part of the week. That's the way it is with all of us. Whether it's urologic subjects or people, we find most engaging the ones we like best. Of all things in urology I like best this subject, much better than urologic engineering!

I have been asked to discuss the paper of Dr. Berneike and Dr. Deming.

As usual Dr. Deming knows what he is talking about—and Dr. Berneike too. No one could have paid that compliment to Professor von Lichtenberg twenty years ago when he took American urologists by storm with his presentation of this subject. He had a flashy account of technique and an impressive—even staggering—number of cases. But in terms of present day appraisal of these matters Professor von Lichtenberg didn't know what he was talking about for he had absolutely no follow-up information concerning any of his patients. The same was true of most reports preceding von Lichtenberg's. They were engrossed in technical details and had little reference to the results obtained. Actually almost half of those old plastic procedures were failures and were followed by secondary nephrectomies.

Dr. Deming and Dr. Berneike know just exactly what was accomplished in all their cases—and it is a fine accomplishment.

I urge that all technical contributions to this subject be appraised only in the light of actual end results as determined by follow-up information and examination at long intervals after operation. I believe *that* particular feature of my original report concerning the Foley Y-plasty gave the operation its position rather than the plan of operation itself. The same appraisal can be applied to the operation Dr. Berneike and Dr. Deming have described. It must be a good operation if it gives such results. But the plan of operation and technique of its performance are important in these things and I believe that is why I am asked to speak.

In respect of these the paper of Dr. Deming and Dr. Berneike brings up five points listed on this lantern slide:

1. Removal of the redundant pelvis.
2. Use of the T-tube splint.
3. Meticulous suturing.
4. Lowering of the ureteropelvic junction to the most dependent part of the pelvis.
5. Gradual funneling of the pelvis into the ureter.

Removal of the redundant pelvis and use of the T-tube splint were emphasized in the paper and the importance of meticulous suturing was indicated. Lowering of the ureteropelvic junction to the most dependent part of the pelvis and gradual funneling of the pelvis into the ureter were not mentioned.

Removal of the redundant pelvis much improves the appearance in the postoperative pyelo-ureterogram, but does not affect the symptomatic or functional result or clearing of infection.

The T-tube drain and splint are better than a splint entering through a nephrotomy, but have no advantage, that I can see, over my plan of a splinting catheter entering through a stab opening in the pelvis and a pyelostomy tube for continuous or interval irrigations. If fenestrations are cut in the splinting catheter over the segment lying in the pelvis it will serve the same good purpose of pelvic drainage served by the T-tube and is more smoothly removed.

Meticulous suturing is of paramount importance. Note that Dr. Deming and Dr. Berneike mention the use of 5-0 chromic catgut sutures. Nonabsorbable material never should be used. Knowing Dr. Deming as I do, I know the sutures were well placed and gave accurate approximation. That is of prime importance. This along with a fundamentally sound plan of operation explains the good results much more than resection of the pelvis or the T-tube.

The operation described puts the ureteropelvic junction at the most dependent part of the pelvis which is an important feature of any operation for this purpose. If high insertion is not corrected a one-way membrane valve similar to the ureterovesical valve will be left. This detail of technique should be more emphasized.

My discussion of this subject would not be complete or typical without reference to the Y-principle in all such operations. Instead of abrupt passage from the big pelvis to the small ureter by end to side anastomosis, the pelvis should be given a V-shaped flap as formed by the limbs of a Y-incision. This V-shaped flap of pelvis should be approximated into a longitudinal incision in the ureter as would be formed by the stem of a Y. The V-shaped flap of pelvis and longitudinal incision in the ureter when accurately approximated make a gradual funnel. This is important.

Dr. Berneike and Dr. Deming have made an excellent contribution showing what a well planned operation and its good performance can accomplish in this exacting field of urologic surgery. Nothing I have said is intended as unfavorable criticism. I only hope my discussion points out important details of technique as I see them, and will be well received by all of you—particularly the authors to whom I am grateful for the opportunity to contribute these remarks—which are an embelishment a little on the order of gilding the lily.

Dr. William J. Engel (Cleveland, O.): I have followed with interest Dr. Davis' reports on intubated ureterotomy since he first presented this procedure in 1943. His continued use of the method evidently has increased his enthusiasm.

We have adopted this operation only to a limited extent because of a reluctance to employ an indwelling rubber ureteral tube for the long period recommended. I believe that an indwelling rubber tube in any hollow viscus acts as a foreign body which produces irritation and an inflammatory reaction and often favors infection. Furthermore, if pressure points exist, actual necrosis of the wall of the viscus may occur. This has been observed in the esophagus and intestinal tract as the result of a Miller-Abbott tube, in the urethra at the penoscrotal junction from a urethral catheter used with traction, and similar damage undoubtedly could occur in the ureter. Dr. Davis notes that strictures have developed where the end of the tube lay in the ureter, and it is reasonable to suppose that the same situation could result at any point where pressure might be exerted against the tube.

We are all familiar with the frequent association of infection and even stone formation in patients who are obliged to have nephrostomy or pyelostomy tubes. Although infection may be controlled partially with today's antibiotics and chemotherapeutic agents, the tissue response to this infection is all too often a fibrosis with subsequent contraction and stricture formation. We have seen cases of late stricture. Dr. Davis reports that some of his failures are due to recurrent stricture; can he say that this is not the result of a foreign body reaction, plus infection, resulting from the prolonged presence of the rubber tube?

I gather from his paper that encrustation of the tube from urinary salts has been somewhat of a problem. I should like to ask if this is always easily controlled by irrigation with special solutions? Also, what part encrustation may play in his cases of recurrent stone formation?

Whether these objections will be overcome by the use of the newer plastic tubing remains to be seen. There is already rather conclusive evidence that urinary salts will not adhere to the plastic surfaces and, while early reports indicate that there is little tissue reaction to this material, I believe the final answer is not yet at hand. The paper of Drs. Brown and Harrison helps to answer some of these points, I think.

If one employs this operation I am sure it is extremely important to observe the precautions and follow the detail to which the author has called attention. I should like to emphasize two points he has made. The first is the importance of maintaining the ureter in a straight line. In one of our patients the splinting tube was brought out through the incision with resulting angulation of the ureter, which now appears to be a point of obstruction. There is recurrent hydronephrosis with stone and intermittent renal pain.

A recent case illustrates the importance of fixing the splinting catheter. The preoperative pyelogram presented a hydronephrosis and displacement of the ureter which was thought to be retrocaval. At operation a congenital type of stricture was disclosed and, though the ureter did pursue a course medially behind the vena cava, it was not a circumcaval ureter. The stricture was divided as Dr. Davis has described, with the Ramstedt principle, and polyethylene tubing was introduced downward into the bladder (later recovered cystoscopically) and upward to the kidney pelvis. We did not introduce a pyelostomy tube nor fix the upper end of the ureteral tube; herein apparently lay our error. The splinting catheter did not maintain its proper position, slipped down until it no longer served its purpose, and had to be removed. Postoperative films show hydronephrosis with obstruction at the point of operation and, while the patient is without significant symptoms, we fear the hydronephrosis may become progressive.

I am sure we have all been searching for a better method of dealing with ureteral strictures and ureteropelvic obstructions and have experienced unsatisfactory results from attempting various plastic procedures. I believe we will all agree that this method suggested by Dr. Davis has a definite appeal and if the plastic tubing will overcome the objections we associated with rubber, I am sure the procedure will receive wide acceptance in solving what has been a difficult problem in urologic surgery.

DR. CHARLES E. RIESER (Atlanta, Ga.): The paper of Doctors Brown and Harrison is timely. I am sure that many in the audience have been curious concerning the workability and efficiency of catheters made of plastic materials. It is only by an accumulation of personal experiences such as those reported here today that proper evaluation of new modalities results.

I should like to confine my remarks to the use of polyethylene catheters employed as a splinting material in the ureteropyeloplasty operations. Previous personal experience using latex rubber splinting tubes, such as the McIver or Cumming types, has been somewhat disappointing due to the deposits of calcareous grit on that portion of the catheter in contact with the urine. This material is deposited as early as the second week postoperatively. This would occur in spite of means prescribed to provide for acidification of the urine.

Since polyethylene seemed so well tolerated by the tissues even when in contact with the urine, its usage as a splinting catheter was suggested. Although my personal experience has been limited to only one case, my impression was not favorable. This material is so rigid and lacking in flexibility that it causes bowing and angulation, two very undesirable features which could vitiate the results of the operation.

Mr. Outwin of C. R. Bard Inc. recently made a new type of splinting catheter nephrostomy tube combination impregnated with silver salt, after the suggestion of Dr. Ockerblad. My experience indicates that this catheter is well tolerated by the tissues, does not encourage deposition of calcareous grit, and allows for the soft flexibility so desirable in splinting materials. However, its usage has been too limited for me to make any dogmatic statements concerning its final efficacy.

DR. SAMUEL A. VEST (Charlottesville, Va.): After hearing Dr. Foley's learned discussion of this subject, I am sure you will agree that no one could be his resident, as was my privilege, without becoming extremely interested in surgical repair of obstructions of the ureteropelvic junction. I personally gained a great deal out of this discussion, but would like to take this opportunity to clarify a few points:

In the first place, it seems to me that this symposium might have well been titled one on the use of splinting tubes because their employment has been particularly emphasized today. It also seems to me that we are more or less divided up into so called "splinters" and "anti-splinters" with the former in the large majority. At our clinic for the past several years, we have used a splinting tube following the repair of these obstructions only on rare occasions and we do not believe that it is indicated in any but the smallest minority of cases. It was my intention to report on this point at this meeting, but inertia prevented such a presentation.

It has been brought out in this symposium that any particular type of operative procedure is not nearly so important as the performance of a correct and meticulous operation. Certain requirements for a good result must be met and these include proper suturing without tension, funneling, an adequate and dependent stoma and fixation of the kidney without angulation of the ureter or pelvis.

I was particularly gratified to note that some of Dr. Deming's cases were done without splinting catheters and that these did just as well as the ones in which the T or splinting tubes were used. It seems to me, and it certainly has been corroborated by our experience, that if no infection is present and if an entirely satisfactory operation can be performed, that a splinting tube of various types is superfluous. It only enhances the chances of infection which leads to more scar tissue. A splinting catheter also produces ischemia at the site of anastamosis leading to further cicatricial tissue. Scar tissue must be avoided at all costs and I know of no better means to eliminate or restrain scar formation to a minimum than to prevent urinary drainage, infection, and the insertion of foreign bodies such as T-tubes or inlying catheters.

With modern antibiotics the general surgeon no longer uses fancy buttons to anastomose the intestine. By using antibiotics he now makes primary end-to-end and side-to-side anastomoses with ease without the use of inner tubes and other appliances. It occurred to us that primary closure of various plastic repairs of the renal pelvis was certainly in order in cases in which no infection was present and a satisfactory operative procedure could be accomplished. It is our conclusion that cases of uninfected primary hydronephrosis do better without such tubes. We simply leave a Penrose drain down to the site of anastomosis overnight. The incisions rarely leak urine and do not become infected. Antibiotics are usually started the morning of operation and are continued several days. Morbidity is shortened as well as hospitalization.

It is admitted that there are some few cases in which the splinting tube, so ably presented by Dr. Davis, is life saving. This is in cases in which a satisfactory plastic procedure is impossible such as long narrow strictures of the lumen or cases in which the ureteral and pelvic wall is thickened by scar tissue. In such instances there is no other way than that devised by Dr. Davis.

I think the individual surgeon should perform the type of plastic procedure in these cases in which he has the most confidence and can do best. At our clinic we find the Y-plasty devised by Dr. Foley to be applicable to the largest number of cases and believe it more nearly answers the desired objective of dependent drainage than the others. We perform this type of procedure with primary closure and without the use of splinting catheters and certainly with excellent postoperative results. It is with these thoughts that I wanted to voice one vote of protest to the idea of taking all cases and assuming that a postoperative splinting tube or catheter is necessary. I would like to emphasize that cases should be selected for the use of such tubes and it is my belief that they are indicated in only a small percentage of cases and should not be used routinely.

Dr. Seymour F. Wilhelm (New York, N. Y.): I agree with Dr. Foley, as expressed a few minutes ago, that the finer variations are not of decisive importance, provided the fundamental principles of plastic renal surgery are followed. We have already heard that the suturing must be carefully done, the stoma must be made wide and placed in the most dependent portion. Above all, the operation should be kept simple.

The question of splinting catheters is not settled in my mind. I have used them a good deal but, in addition, I have also done a nephropexy in these cases to fix the kidney, so that the ureter and the pelvis remain in a straight line.

(Slide) I prefer to do either a Foley Y-plastic or a side-to-side type of anastomosis, such as is shown here, a simple anastomosis somewhat similar to von Lichtenberg's procedure in which the stoma can be made as wide as one wants it. In these cases, I have routinely employed the splinting catheter making the new opening at the most dependent portion of the pelvis, and have also used a nephrostomy tube. I have now operated on 11 such cases over the course of the last 13 years, with one failure in which nephrectomy was necessary. The other 10 cases have been followed, the longest now being a little over 13 years.

(Slide) This is an excretory urogram of a man made in 1937. I did a simple side-to-side anastomosis on his single hydronephrotic kidney. I had given up doing resections and plications of the pelvis which I had formerly done. All I did was to make a wide stoma at the lowermost portion of the pelvis. This man has been working steadily as a post office clerk for the last 13 years and is perfectly well. This is a slide of the excretory urogram after this time.

In closing, I want again to congratulate the authors and the discussers of these splendid papers.

Dr. Clyde L. Deming (New Haven, Conn.): I should like to thank Dr. Foley for his kindly discussion of our paper, and I would like to say that we did not attempt this procedure to replace Dr. Foley's Y-plasty procedure, because we have great respect for it and we appreciate it as a contribution.

Dr. Vest has divided us into splinterers and non-splinterers. I feel like the fellow on the football field; when I am on the offensive, I do not use a splint, but when I am on the defensive, I am going to use a splint.

This series of cases which we have given you represents the treatment of rather large hydronephroses which have had either aberrant vessels or a rather tight, prolonged, elongated stricture. We felt that we would like to produce a result which would give the final requisites which Dr. Foley placed on the screen. We are in full agreement with his statements.

We felt that one cannot do a nephrostomy without some injury to the cortex of the kidney. This injury involves nephrons and groups of nephrons which heal with fibrous tissue leaving ischemic areas. It must heal that way. The area may be small. Whether it is important or not, I do not know, but I would prefer to leave the cortex of the kidney without a scar.

Our experience with drainage of the pelvis in these cases has not been satisfactory. We prefer other methods of drainage because there is always a little leakage at that area and there is a little pooling of the drainage.

We have given you the bad as well as the good results in our cases. We feel that the T-tube can be used in cases of infections with hydronephrosis and that the end results desired can be obtained by removal of the excess pelvis with a good funnel-shaped pelvic outlet and a 100 per cent functioning kidney cortex.

DR. DAVID M. DAVIS (Philadelphia, Pa.): Intubated ureterotomy as described today stands without any competition whatever in a certain number of cases, namely, those in which the strictures of the ureter are multiple or in which a stricture is so long that no other operation ever known or described can be used. To this extent, it may in such cases be (and has been in a number of instances) an absolutely life-saving procedure. Our experience in such cases, and the excellent results obtained, of course made us wonder whether the same procedure, recommended by its simplicity, could not be used in other kinds of obstruction, and here, of course, it comes in competition with other methods.

It is easy to see from what has been said today that other methods produce excellent results also, provided the proper principles are followed. We have used intubated ureterotomy in a large variety of obstructions and we find that our results are good. I do not believe that any frustration has been because of any recurrent stones. Recurrent strictures have been very few and they have usually been in the cases where the infection was extremely severe at the time of operation, and where it was not possible to eliminate it as rapidly and as completely as one would like afterwards.

I have not used the polyethylene tubes for the same reason that one other discusser has mentioned, namely, I thought they were too rigid and stiff. The polyvinyl tubes will be much more suitable.

I would like, in view of the situation, to show three cases which I will run through quickly. (Slide) This first case is in a little girl 18 months of age and, as you will see, there is, in the panel to the left, a very large hydronephrosis of the right kidney and quite a large hydronephrosis of the left kidney. There was a stenosis of the ureteral meatus so that a No. 4 catheter was inserted with difficulty. There is also another area narrowing of the ureteropelvic junction. This is a fairly long narrowing.

The other panel shows the situation after the upper stricture had been intubated for a period of four weeks.

(Slide) At the end of 4 weeks, the lower obstruction was also treated. The ureter was exposed lateral to the bladder, the bladder was then opened and the ureteral meatus and the ureter incised until a No. 12 tube could be inserted. This tube was left in place, emerging through a cystotomy wound, for another four weeks.

The other pictures show the state of the ureter at the end of the second four-week period. It has now been restored to a very excellent caliber.

(Slide) This picture was taken 4 months after the last operation. At the time this picture was taken, the child was quite well, with sterile urine. A No. 10 bulb ascended the ureter of this 18-months-old child all the way to the kidney without any resistance whatever. The hydronephrosis is already considerably reduced.

(Slide) This is a case of small hydronephrosis which produced very serious difficulties. The young woman had had diffuse abdominal pain, anorexia, nausea and vomiting over a period of 2½ years, which had reduced her to a weight of 92 pounds and caused severe mental depression. It seemed incredible that a small hydronephrosis could do so much harm, but the second picture shows how the ureter runs through an 180° curve after it leaves the pelvis. The third picture shows that there is marked retention in the pelvis at the end of 10 minutes after the withdrawal of the ureteral catheter.

(Slide) The picture on the left shows the intubating tube passing through the entire length of the ureter. The second picture shows the pelvis already reduced in size, as outlined by skiodan solution injected through the drainage tube.

The third picture shows the ureter after the removal of the ureteral splint and, as you see, it follows a straight course throughout and the ureteropelvic junction is well formed. Immediately after that picture was taken, the pelvic tube was clamped and the patient stood erect for 10 minutes. The last picture shows her pelvis emptied completely. Since that operation, she has remained perfectly well, with sterile urine, and has gained 40 pounds.

(Slide) This is another hydronephrosis with ureteropelvic obstruction and three stones in the middle calyces. The third picture shows the 10-minute emptying film and you can see that there is marked retention in the pelvis.

The picture to the left shows the excretory urogram. The next one shows the entire ureter intubated. In this case, the intubating tube was brought out through a nephrotomy incision because we had to make two nephrotomies in order to remove the stones in the middle calyces.

The third picture shows the ureter after the intubating tube had been brought upward into the pelvis, and you see it has an excellent appearance and the ureteropelvic junction now looks normal. This tube was left in that position and clamped; there was no leakage of urine and, at the end of 10 minutes, the fourth picture shows that the pelvis was completely emptied. This woman also has remained perfectly well for a period of almost a year, the urine being sterile at all times.

DR. J. HARTWELL HARRISON (Boston, Mass.): Apparently Dr. Brown covered all of the aspects of his subject for no questions seem to have arisen. However, I must make one or two points with reference to misconceptions which seem to have arisen: One, namely, that no deposition of urinary salts will occur on plastic catheters. That, we have not found to be true. Dr. Brown did not say this but that impression seems to have prevailed in subsequent discussions.

The polyvinyl plastics that we have made into catheters have not been pure and they have the increased malleability which Dr. Davis referred to because of the addition of a plasticizer, which is a compound, to us of unknown origin because it is a secret of the trade. We do know that the presence of that compound, which confers malleability to these catheters, constitutes the presence of an impurity and as a result of that, deposition of calcium salts will occur. However, said deposition, or tendency to it, is less than it is, by far, with the rubber catheter.

With reference to polyethylene, Dr. Davis' point is well taken, that to use it as a splint, if it is a large tube, it would be too stiff, but in the smaller tubes greater malleability is present and, knowing the efficacy of the larger lumen which is present, I believe for those who wish to use splints in the repair of hydronephrosis and strictures of the ureter, that polyethylene may be of value.

(Slide) This is a cysto-urethrogram of a 9-year-old boy whom we saw 18 months after fracture of the pelvis and a rupture of the urethra. Apparently at the time, or shortly after his injury, a urethrogram had been made with lipiodol, and we see that posteriorly behind the bladder. The area of stricture is quite apparent. At this time he had several calculi in his bladder.

A combined abdomino-perineal repair of this stricture was carried out, the calculi being removed and the continuity of the urethra restored by the use of a polyvinyl acetate tubing. This tubing was left in place for 3 weeks, and upon removal, definite deposition of calcium salts on the polyvinyl tube was found. We have not experienced a similar deposition of calcium salts on polyethylene tubing, but Swenson, at Children's Hospital, who has utilized this tubing for the suprapubic drainage of children with paralytic bladders, has found the presence of calcium salts in a small degree after a period of 3 weeks. This is more likely to occur in those cases where there is gross infection with urea-splitting organisms.

Dr. Brown failed to mention the fact that, 2 years ago when we first used polyethylene tubing, he converted this tubing into catheters, ureteral and urethral, in a shop in his basement, and they have been of great value for drainage of 1 to 3 weeks' duration.

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CYTODYNAMIC PROPERTIES OF URINARY NEOPLASMS: II. MAINTENANCE OF "HYPERNEPHROMA" IN VITRO

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In a previous communication, Bunge and Stein[1] reported the in vitro growth of a ureteral neoplasm in both natural (embryo extract and human umbilical cord serum) and synthetic (White) media.

Since each cell type responds characteristically to a similar environment, it may be assumed that the structural and functional states of a cell depend on its cytogenetic constitution as well as on the physicochemical conditions of the medium in which it grows. Cells removed from their environment (medium) are abstract entities. Any study of cellular dynamics demands a system which embraces both the cell and medium in a functional aggregate.

To apply the "cell-medium" concept to cytopathology requires a new approach, consisting of techniques for exploring both the structural and functional components of a cell. Under proper physical and chemical conditions, cells in tissue culture can be kept viable indefinitely in vitro. This permits tissues to be studied not only as static entities but as functional units capable of growth and aging, and of reacting to disease-producing and therapeutic agents. The lack of agreement in classification of "hypernephromas," the peculiarities of their response to treatment and their varied biochemical characteristics prompted an investigation of the possibilities of this new tissue-culture approach to the cytodynamic problems involved.

It has been shown by Fell,[2] Martinovitch,[3] and Hanks,[4] that both embryonal and adult tissues can be maintained in a differentiated and organized state in vitro. It is the purpose of this communication to report the maintenance in tissue-culture (Fell's method) of a human hypernephroma.

N. M., a white woman, aged 67 years, complained of total gross hematuria of 24 hours' duration. Examination revealed a large, nontender, smooth and fixed mass in the right flank. The urine contained many red blood cells. The retrograde pyelogram showed a large space-occupying lesion at the lower pole of the right kidney. A preoperative diagnosis of hypernephroma was made; the mass and kidney were removed. Histological section revealed a typical clear-cell carcinoma of the kidney (fig. 1, *A*).

MATERIALS AND METHODS

The specimen obtained for culture was received from the operating room under sterile conditions and was explanted within 2 hours after removal. The tissue was cut into pieces about 1 mm. cube and transferred, until ready for culture, to a watch glass containing Tyrode's solution to which 200 units of penicillin and 2 mg. of streptomycin per milliliters had been added.

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[1] Bunge, R. G., and Stein, R. J.: J. Urol; **64:** 646, 1950.
[2] Fell, H. B. and Robison, R.: Biochem. J., **22:** 767, 1929.
[3] Martinovitch, P. N.: *Proc.* Royal Soc. Lond., Series B, **128:** 138, 1939.
[4] Hanks, J.: Personal communication.

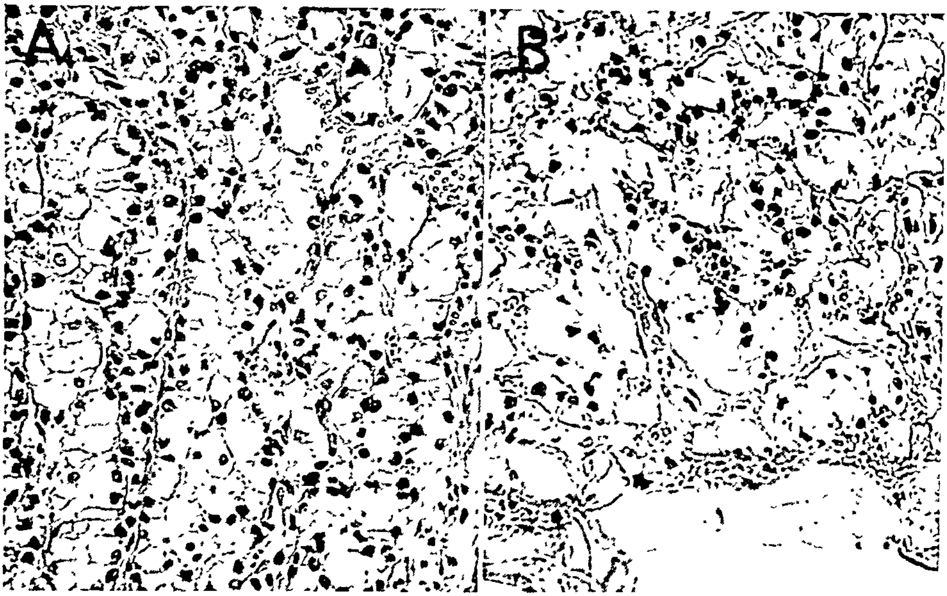

FIG. 1. *A*, control section of clear cell carcinoma of kidney before explantation into tissue culture. (H & E stain, × 200.) *B*, histology of explant after 14 days in tissue culture. Note characteristic architecture of clear cell carcinoma. (H & E stain, × 200.)

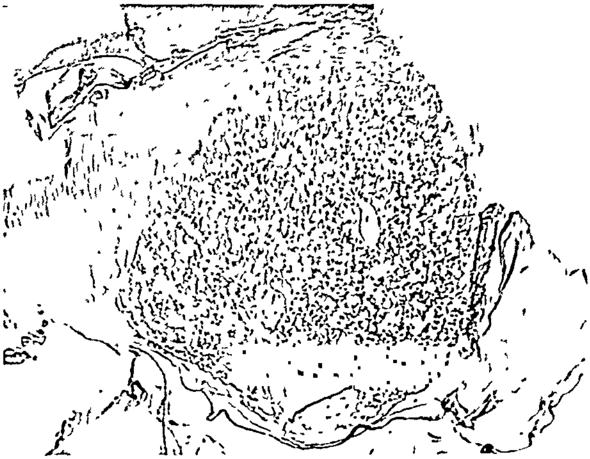

FIG. 2. Photomicrograph showing explant of clear cell carcinoma incorporated in clot of medium. (H & E stain, X 10)

The cultures were made in Carrel D35 flasks as follows: Ten drops of rooster plasma and ten drops of 50 per cent chick embryo extract were introduced into each flask and allowed to clot. Either two or three explants were placed on the surface of the clot and incubated. Since Martinovitch[3] has demonstrated that tissue incubated in vitro at subnormal temperatures (34°) remained viable for eighty days as compared to thirty days at 37C, the "hypernephroma" explants were maintained at 35C.

OBSERVATIONS

After 5 days' incubation, the explants exhibited some fibroblastic proliferation at the periphery. After fourteen days in vitro the explants were removed from the flasks, fixed in Bouin's fluid. sectioned and stained with hematoxylin and eosin. Sections exhibited a typical clear-cell carcinoma, the cyto-architecture of which was similar to that of the original tumor (figs. 1, *B* and 2).

DISCUSSION

These results indicate that tissue culture methods can well be applied to the study of "hypernephroma." The ability to maintain such a renal neoplasm in a viable state for prolonged periods provides a simultaneous approach to the study of the effect of the tumor on the medium and of medium on the tumor. This presents interesting possibilities for study of the mechanism whereby the medium determines the functional activity and differentiation of main cell types, and how growth-promoting and growth-inhibiting factors affect the cellular protoplasm. Classic histology has provided many abstractions which were of immense value in the development of our knowledge of renal lesions, even though it divorced structure from function. In vitro methods offer a means whereby structure and function may be correlated.

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PRIMARY LYMPHOSARCOMATOSIS OF KIDNEYS, ADRENAL GLANDS AND PERIRENAL ADIPOSE TISSUE

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It is a well-known fact that the kidney is a favorite seat of metastatic lymphosarcoma. On the other hand, the existence of primary lymphosarcoma of the kidney is uncertain.[1]

Elmer and Boylan[2] published a case of lymphosarcoma which appeared to be confined to the kidney, both clinically and at operation, although definite proof of a primary renal involvement was lacking because at autopsy the disease had become generalized.

Gibson[3] reported 3 cases of lymphomatous involvement of the kidney which clinically pointed to the presence of a primary renal neoplasm, but which either at operation or at autopsy were found to be massive retroperitoneal lymphosarcoma with secondary involvement of the kidneys. Gibson stated that there are approximately 650 cases of renal tumor in the American Registry of Pathology and quotes a personal communication from its scientific director, ". . . We have 5 cases that are coded lymphosarcoma, kidney. In looking these over, however, while 3 of them were nephrectomies, they were all, so far as we can determine, a part of a systemic process." Gibson goes on to state that lymphosarcoma of the kidney is secondary to a primary focus elsewhere, and that renal lymphosarcomatosis rather than lymphosarcoma of the kidney is a more appropriate terminology.

Puente Duany[4] describes two types of diffuse lymphomatous involvement of the kidney: 1) the "capsular", in which the kidney is engulfed by the tumor as by a flow of lava which surrounds it and may invade the cortex; and 2) "bilateral renal diffuse lymphosarcomatosis," in which there is a uniform infiltration of the renal parenchyma by the lymphomatous cells, resulting in a corresponding enlargement of the organ without alteration of the shape. He found only 17 cases of the bilateral diffuse type in the literature, and most of these occurred in infants.

The present case is one of lymphosarcoma confined to a symmetrical, bilateral massive involvement of the kidney and adrenal areas, with one solitary, small metastatic subcapsular nodule in the liver.

We believe that this case is interesting from an anatomical and clinical standpoint, and we think that its occurrence supports the theoretical possibility of the existence of a primary lymphosarcoma in this region.

Reviewed in the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are the result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

[1] Ewing, J.: Neoplastic Diseases. Philadelphia: W. B. Saunders Co., 1940.

[2] Elmer, R. F. and Boylan, C. E.: Reticular sarcoma of the kidney. Ill. Med. J., **65:** 83–85, 1934.

[3] Gibson, T. E.: Lymphosarcoma of the kidney. J. Urol., **60:** 838–854, 1948.

[4] Puente Duany, N.: Linfosarcoma y Linfosarcomatosis de los Rinones. Rev. de med. trop. y parasitol, bacteriol, **6:** 213–251; 303–326, 1940.

CASE REPORT

A white man, aged 67, was first admitted to the hospital on November 24, 1949, complaining of generalized weakness, loss of appetite and anterior chest pain. He stated that the symptoms had appeared only 5 weeks prior to the hospital admission but he had noted that in the past 3 months he had lost 22 pounds in weight. The chest pain was quite severe, radiating through his back and down his spine to the left hip and leg. Two weeks prior to admission severe nausea and vomiting had started.

Past history revealed recurrent attacks of bronchitis and a period of hospitalization in 1946 for coronary thrombosis. His father had died at the age of 42, of Bright's disease, and one brother had died at 58 of kidney disease (not better identified).

The physical examination revealed a pale and dyspneic man who appeared chronically ill. The contour of the thorax suggested emphysema. Lung fields were clear and hyperresonant throughout. The blood pressure was 190/100, pulse 76, regular, and heart enlarged to the left. The abdomen was obese. The lower edge of the liver extended one fingersbreadth below the right costal margin. The spleen was not palpable. One small, soft, movable lymph node, 1 cm. in diameter and nontender, was palpated in the right axilla. Two small discrete lymph nodes were noted at the base of the right anterior triangle of the neck.

Laboratory data on admission: Urinalysis: Amber color, acid, specific gravity 1.010, albumin 4-plus, glucose—none found; microscopically 6 to 8 white blood cells/per high power field, with hyaline casts. Blood: Red blood cells 3,690,000; hemoglobin 74 per cent, white blood cells 8,950; differential,—55 per cent polymorphonuclears, 40 per cent lymphocytes, 1 per cent monocytes and 4 per cent eosinophils. Sedimentation rate: 34 mm. Serology: Negative. Blood sugar, 121 mg. per cent; blood urea nitrogen, 45.7 mg. per cent; creatinine, 5.5 mg. per cent.

X-rays of the spine showed osteo-arthritic changes involving the lumbosacral segment. Excretory urography showed very little concentration of the dye in the right kidney pelvis. There was no definite evidence of any concentration of the dye in the left kidney. Very little of the dye was in the urinary bladder. No definite statement about the renal pelves and calyces could be made because of the poor functioning with diodrast.

Other pertinent laboratory data follow: Bence-Jones protein in the urine: None found. Acid phosphatase, 1.83 units; alkaline phosphatase, 3.06 units. Repeated urinalyses showed hypo- and isosthenuria, constant presence of albumin, hyaline casts and white cells. Red blood cells appeared in the sediment on December 24.

Hematologic studies: December ninth: Red blood cells 3,510,000; white blood cells 6,350; hematocrit 33; hemoglobin 70 per cent. Differential: Segmented 64; lymphocytes 30; monocytes 3; eosinophils 3.

December nineteenth: Red blood cells 3,480,000; white blood cells 4,500; hematocrit 34; hemoglobin 68 per cent. Differential: Band forms 1; segmented 86; lymphocytes 12; eosinophils 1.

December twenty-ninth: Red blood cells 3,250,000; white blood cells 13,000; hematocrit 32; hemoglobin 65 per cent. Differential: Band forms 3; segmented 71; lymphocytes 24; eosinophils 2.

January third: Red blood cells 3,650,000; white blood cells 5,700; hematocrit 35; hemoglobin 68 per cent. Differential: Band forms 2; segmented 77; lymphocytes 21.

The patient had an irreversible, downhill course despite supportive treatment and blood transfusions. Nausea and vomiting were continuous. There was a gradual rise in the blood urea nitrogen and blood phosphorus, accompanied by a fall of the blood calcium and of the CO_2 combining power. A mass was felt in the left upper quadrant in the region of the left kidney; but the general condition of the patient did not warrant retrograde pyelographic studies. After about one month of hospitalization gross hematuria was present and on December 26, 1949, the urinary bladder was found to be distended with blood clots. At that time cystoscopic removal of the blood clots and a transurethral resection of a recent infarct of the prostate gland (point of bleeding) were performed. Immediately postoperatively he appeared somewhat improved; however, on December 29, the blood urea nitrogen had risen to 92 mg. per cent and the patient expired quietly 5 days thereafter.

The autopsy revealed an extensive myocardial fibrosis due to atheromatous changes of both coronary arteries (weight of the heart 570 gm.), and a diffuse recent pneumonic process (right and left lower lobes).

The liver weighed 2000 gm., unaltered in consistency and not remarkable except for a well-defined nodule, moderately resilient and measuring 1.5 cm. in average diameter. The nodule was found at the insertion of the falciform ligament at the antero-inferior edge of the organ.

The soft spleen weighed 250 gm. The capsule was slightly wrinkled; a large amount of pulp was scraped away on the knife.

Small, soft lymph nodes were found on both sides of the neck and in the right axillary region. They were less than 2 cm. in maximum diameter. On section the cut surface of the lymph nodes was smooth and pinkish-gray, with well-defined hili. The mediastinal, mesenteric, inguinal and lumbo-aortic lymph nodes were not remarkable.

Both adrenal glands were firm and enlarged. The left weighed 25 gm.; the right 20 gm. On section the cortex appeared to be replaced by gray lardaceous tissue. The medulla, although reduced in width (considering the size of the organ), was still recognizable as such, and reddish-brown in color. The peri-adrenal adipose tissue was increased in thickness and firm, and merged with the perirenal adipose tissue which was similarly firm, gray and studded with areas of hemorrhage.

Both kidneys were uniformly increased in size. The right kidney weighed 575 gm.; the left kidney 650 gm. The thickened, lardaceous capsule was stripped with slight difficulty, revealing a smooth external surface, pale pink in color and studded with hemorrhagic areas, the largest of which measured 2 cm. in maximum diameter. These hemorrhages were ill defined and were not noted on the cut surface. The pelves were not dilated. The lining epithelium of the pelves was slightly granular and frankly hemorrhagic. The cut surface of both kidneys showed well differentiated cortex and medulla, the latter reddish-brown with prominent pyramids (fig. 1). The cortices were increased in thickness and firm, almost lardaceous, their pale pink color sharply contrasting with the adjacent medulla. No infarcts were noted. The pelvic fat was firm, gray, and increased in amount. The ureters were normal in caliber, with granular, pinkish-gray lining.

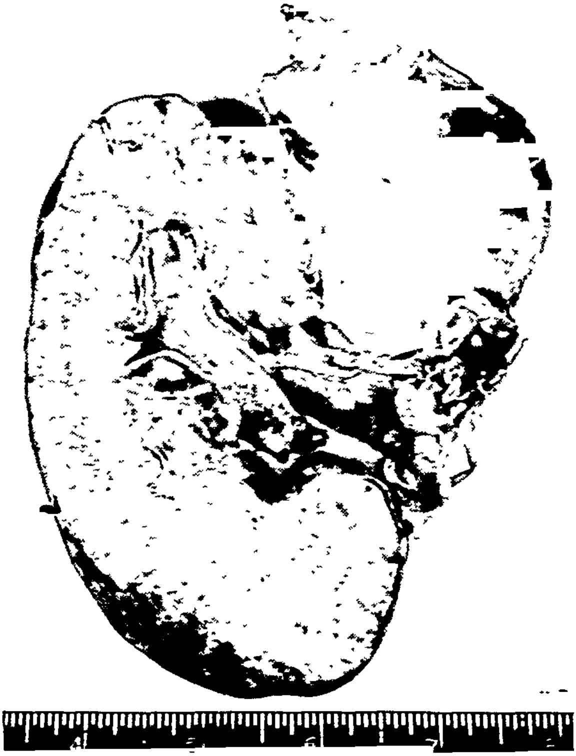

FIG. 1. Left kidney, cut surface, posterior view, including adrenal gland. Massive lymphomatous involvement.

The urinary bladder was contracted, lined with pinkish-brown mucosa. The prostate gland was soft. Its cut surface was smooth and gray, with a few periurethral hemorrhagic striations.

Abdominal aorta, the inferior vena cava, the pancreas and the mesentery were identified, dissected, and found not involved in the neoplastic process even in the portion contiguous to the renal masses. Both renal arteries were patent throughout.

No significant macroscopic findings were noted in the other organs and systems.

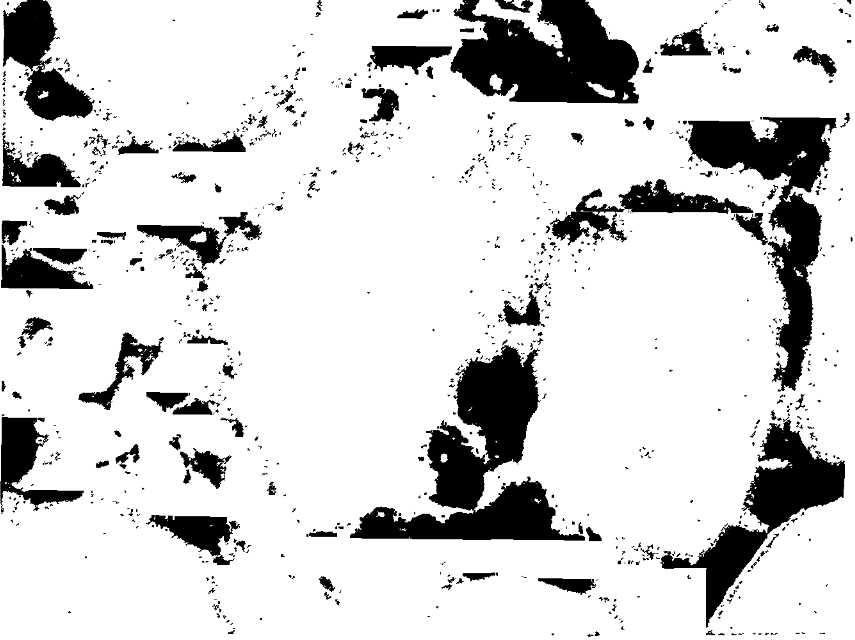

Fig. 2. Lymphomatous metaplasia, perirenal fat. H. and E. stain. × 352

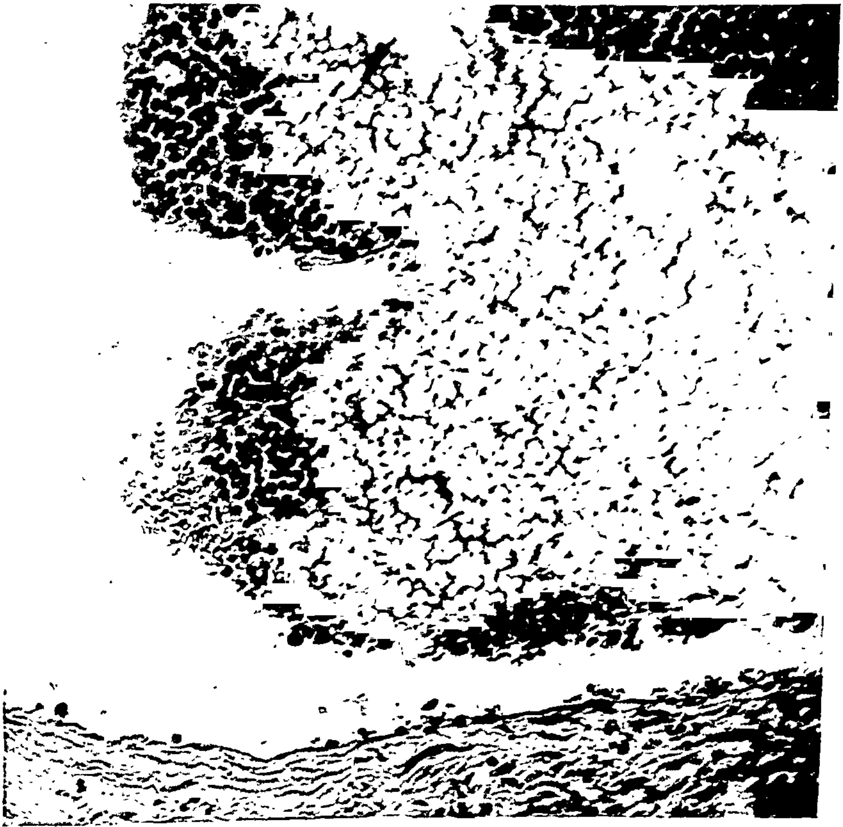

Fig. 3. Tumor embolus in large vein, peri-adrenal fat. H. and E. stain. × 96

Histological examination (only pertinent findings are reported): Periadrenal, perirenal fatty tissues and capsule of the kidneys showed massive lymphomatous metaplasia and hemorrhages (fig. 2) and presence of lymphomatous masses in the veins, with disruption of the vessel wall (fig. 3).

Both kidneys displayed pronounced lymphomatous involvement of cortex and pelvic fat (fig. 4). The cells were typical lymphocytes (medium to large size). Mitoses were very rare. The same process was noted in lesser degree in the medulla. The lymphocytes were found infiltrating the interstitial tissues and crowding out and extensively replacing the parenchyma.

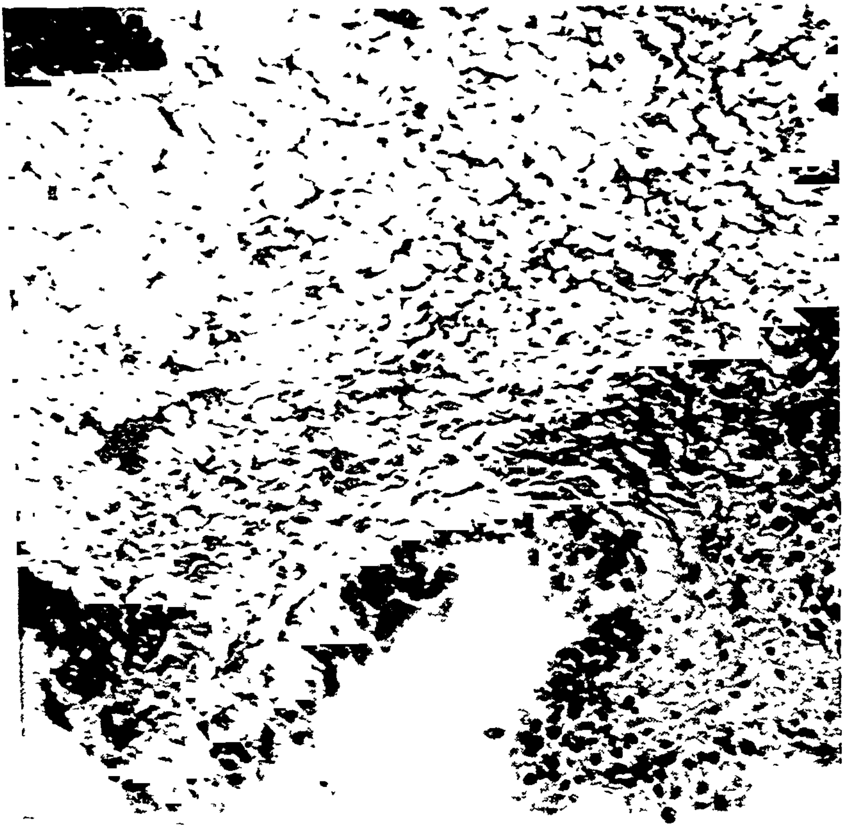

FIG. 4. Lymphamatous infiltration of renal pelvis H and E. stain. × 96

The glomeruli were decreased in number and compressed. Some of the tubules (distal convoluted) contained brown granular casts and showed occasional necrosis of the lining epithelium. The small arteries showed moderate sclerotic changes of the wall. Extensive hemorrhages beneath the lining of the pelves were noted.

The nodule in the liver was constituted by solid sheets of fairly uniform cells belonging to the lymphoid series. Other sections of the liver showed mild congestion about the efferent vein.

Sections of various lymph nodes showed a quite uniform picture so that one description is sufficient: Structure of the nodes was preserved. The cortical lymph follicles were normal in size, the peripheral sinus contained a few mononuclear elements, sinusoids in the hilus unaltered.

The structure of the spleen was preserved. The lymph follicles were small. The red pulp was moderately congested.

There was a moderate degree of fat replacement in the marrow substance; immature forms of granulocytic and erythroid series were recognizable. The wall of the small vessels did not show changes of note.

The other microscopic findings (heart and lung) confirmed the previous gross description.

The final diagnoses were: 1) lymphosarcoma of adrenal glands, peri-adrenal and perirenal adipose tissue, kidneys, massive—and of liver (one small nodule); 2) pneumonia, lobular, right and left lower lobes; 3) arteriosclerotic heart disease, with extensive replacement fibrosis.

Death was attributed to the lymphosarcomatous process with uremia, and was contributed to by the bilateral lobular pneumonia.

DISCUSSION

The pathologic findings just reported were those of a lymphoma involving both kidneys and adrenal glands, together with extreme lymphomatous metaplasia of the peri-adrenal and perirenal fat. A solitary, obviously metastatic, small, subcapsular lymphomatous nodule in the liver was also noted. The lymphomatous process was not present anywhere else in the body. The lymphatic system was found unaltered grossly and microscopically. The spleen (250 gm.) did not reveal changes of note; the bone marrow of the bones examined did not show any suggestion of leukemic infiltration and the x-ray findings of the long bones were not relevant.

These findings are worthwhile emphasizing because they are important for the exact nosological interpretation of the case and because they will throw some light on the problem of the origin of the lymphomatous disease. As mentioned before, the cortex of the kidney was extensively infiltrated by the lymphomatous elements, whereas the medulla was relatively free of tumor. The lymphomatous metaplasia was present again in the fat of the renal pelvis. Similar distribution was noted in the adrenal glands, where the medulla was relatively less involved than the cortex. Perirenal and periadrenal fatty tissue were the site of a global lymphomatous metaplasia.

Apparently the kidneys were not the main primary focus of the disease. It is our belief that the process initiated in the adrenal cortex and/or the peri-adrenal and perirenal adipose tissue. Strict relationship between adrenal cortex and lymphopoiesis has been demonstrated many times in the human pathology and in the field of experimentation.[5] Some foci containing lymphocytes have often been noted in the adrenal glands of man. They are especially common in the so-called primary contracted adrenal gland but they are also seen in connection with a great variety of other diseases, usually being noted as an incidental finding at autopsy. The stroma of human adrenal gland often contains ordinary fat cells, and transitional stages between the latter and the adrenal cortical cells with comparatively large lipid granules are also observed. On the other hand, the multiple developmental potentialities of the adipose tissue as a whole and of some dedifferentiated portion of it (embryonal, brown fat) are of common knowledge.[6] The literature reports several instances of a myelo- and lymphopoiesis in the renal pelvis of man, in most of the cases being only a localization of a more generalized leukemic disease, and only in a few instances being an isolated occurrence.

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[5] Selye, H. and Stone, H.: Hormonally induced transformation of adrenal into myeloid tissue. Am. J. Path., 26: 211-225, 1950.

It is important to mention the histologic findings of our case because the lymphomatous proliferation was found in one of the locations which anatomically and functionally constitute a unit (perirenal and periadrenal and pelvic fat).

The extensive, symmetrical, massive involvement of the extrarenal structures makes us think that the latter rather than the kidney itself represent the primary focus. No further speculation or differentiation is deemed necessary because adrenal cortical tissue, peri-adrenal fat and fatty tissue of the renal pelves show great structural similarity, and in our case can be postulated conjointly as the original site of the lymphoma.

From a clinical viewpoint it might be very difficult at times to establish the diagnosis of lymphosarcoma of the kidneys and this is demonstrated once more by the analysis of our case. The hematological studies and the histologic appearance of the bone marrow did not disclose any evidence of lymphatic leukemia; and no symptoms of adrenal cortical insufficiency of chronic type were noted in spite of the extensive bilateral lymphomatous involvement of the adrenal cortices. The urinary findings were not characteristic, but rather suggested a chronic glomerulonephritis or a moderately severe arteriolar nephrosclerosis; the hematuria was not constant and was due to a large extent to another pathologic condition (infarction of the prostate gland). The most significant clinical findings were represented by the progressive retention of nonprotein nitrogen and by the decreased concentration and excretion of diodrast following excretory urography. Both changes were caused by the diffuse cellular infiltration in the intertubular spaces and by the involvement of the periglomerular structures, as is noted not rarely in leukemia.[7]

This type of severe, irreversible, renal impairment is, in our opinion, the only indication for suspecting the presence of such a pathological picture in patients with uremia when pyelographic studies fail to reveal abnormalities and/or obstructive lesions in the renal pelves and in the lower genito-urinary tract.

[6] Petri, E.: Ueber Blutzellherde im Fettgewebe des Erwachsenen und ihre Bedeutung für die Neubildung der weissen und roten Lymphknoten. Wirch. Arch. 258: 37–51, 1925.

[7] Bell, E. T.: Renal Diseases. Philadelphia: Lea & Febiger, 1946.

SUMMARY

A case of lymphosarcoma involving only both kidneys and adrenal glands and surrounding adipose tissue has been reported.

The case supports the concept of "primary" bilateral renal diffuse lymphosarcomatosis (Gibson).

The possibility that the lymphoma originated "sensu strictiori" from the perirenal fat has been discussed.

The clinical picture with progressive irreversible renal failure has been emphasized.

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URETERAL ECTOPIA ASSOCIATED WITH RENAL DYSTOPIA

RALPH R. LANDES

Among the more than four hundred cases of ureteral ectopia thus far reported, only four were associated with renal dystopia. Two of these were congenital solitary pelvic kidneys and two were horseshoe kidneys with ectopic openings of one ureter.

The present case is the fifth reported instance of a dystopic kidney drained by a ureter with an ectopic orifice.

CASE REPORT

W. H. Jr., a well developed boy of 6 years, was brought to the office on May 31, 1949. His mother stated that the child had been found to have large quantities of pus in his urine at every examination since the age of 2 years. Aside from a severe burn of his abdomen which was incurred 2 years previously, the child had been unusually healthy. His appetite had been good, his weight gain and development had been normal and he had developed bladder control at an early age. He had no frequency or other urinary complaints. During the past 3 years he had been treated periodically with sulfonamides and penicillin and had had his tonsils removed in the hope of eradicating the pyuria.

Physical examination: Temperature, normal; blood pressure, 115/70. Extensive scarring was present on the skin of the abdomen due to a burn by scalding water 2 years previously. Otherwise, the physical examination was negative. In particular there was no flank tenderness and there were no palpable abdominal masses; the external genitalia were normal and both testicles were present in the scrotum; and the vasa were normal to palpation. The child was observed to void with a full forceful stream.

Urinalysis showed a turbid specimen of acid reaction, 2 plus albumin and 25–30 pus cells in each high power field.

Excretory urography revealed a well functioning, normal appearing left kidney and ureter. The renal shadow on the right was absent and no excretion of contrast medium was observed on the right in 60 minutes. The cystogram showed a sharp extrinsic pressure defect of its right margin (fig. 1A). On the basis of these findings a tentative diagnosis of hydronephrosis of a nonfunctioning pelvic right kidney was made. It was believed that a normally situated kidney with hydronephrosis large enough to cause such a pressure defect of the bladder would certainly be palpable.

The child was admitted to the hospital on the following day. Further laboratory studies revealed a red blood cell count of 3.5 million, hemoglobin of 10 gm., and a leukocyte count of 7,000 with a normal differential count. The blood nonprotein nitrogen was 32 mg. per 100 cc.

Cystoscopy was performed under vinethane-ether anesthesia on the day following admission to the hospital. The bladder mucosa was normal and the

Read at annual meeting, Mid-Atlantic Section, Hot Springs, Va., March 23, 1950.

pressure defect of the right lateral wall was evident. The left ureteral orifice was normally situated and clear efflux was seen. The interureteric ridge was not prominent on the left and faded medially into the vesical neck. No orifice was seen on the right. The prostatic urethra was edematous as was the verumontanum. The utricular opening was prominent and the catheter was passed into it for 1.5 cm. The orifices of the ejaculatory ducts could not be made out. On the right lateral wall of the urethra a rather gaping orifice was seen. It was probed with an 4F ureteral catheter which passed upward for its entire length with minimal urging. About 250 cc of turbid urine was aspirated. Ninety cubic centimeters of contrast medium was then injected through the catheter and films were taken (fig. 1,*B* and *C*). The catheter was left indwelling. The diagnosis of right hydronephrotic pelvic kidney with an ectopic ureteral orifice was made.

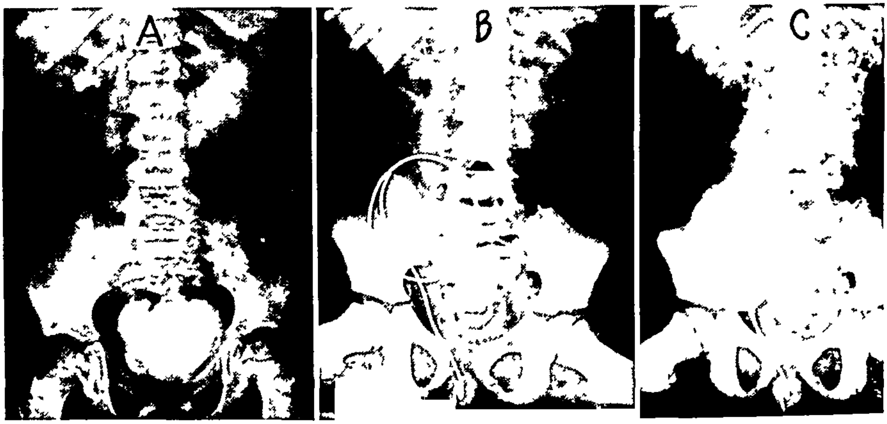

FIG. 1. *A*, excretory urogram showing normal left kidney and pressure defect of bladder. *B*, showing coiled catheter in pelvic kidney *C*, showing hydronephrotic right kidney and urethral origin of ureter

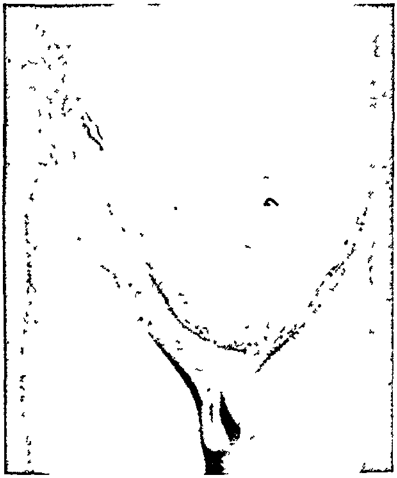

FIG 2 Indicating incision

On culture, the urine obtained from the hydronephrotic kidney contained nonhemolytic streptococci and Aerobacter aerogenes.

Two days later surgery was performed under ether anesthesia. A curved right inguinal incision was made from 3 cm. medial to the anterior superior iliac spine to just above the pubic tubercle (fig. 2). The aponeurosis of the external oblique was incised and the incision was carried partially across the rectus fascia. The external and internal oblique and the transverse abdominal muscles were incised in the direction of the wound. The deep inferior epigastric vessels were isolated, clamped, cut and ligated. The transversalis fascia was opened and the peritoneum was exposed and displaced medially exposing the collapsed hydronephrotic kidney overlying the iliac vessels and extending down into the pelvis. It was easily freed from its bed by blunt dissection exposing its vessels which arose from the iliacs and which entered the renal remnant laterally. The ureter was of normal caliber and entered the pelvis at its lateral margin. Its insertion into the pelvis was high and angulated. The vessels and ureter were individually clamped, cut and ligated and the organ was removed. The transversalis fascia was closed with interrupted OO chromic catgut. The muscles were approximated loosely with fine plain catgut horizontal mattress sutures. The external oblique and rectus fascia were closed with interrupted double-o chromic catgut and the skin, with silk. The wound was not drained.

"The specimen was a thin walled sac measuring 20 cm. in length and 8 cm. in width. The wall measured 1 mm. in thickness. The inner lining was smooth, markedly injected and pale blue-gray. The sections showed the wall made up of dense fibrous tissue. Part of one surface was covered by flattened epithelium resembling the lining of the kidney pelvis. Some chronic inflammatory cells were seen. No true kidney tissue was noted." (Dr. Thomas J. Moran, pathologist at Memorial Hospital.)

The patient's postoperative course was uneventful and he was discharged on the seventh postoperative day. The urine was free of pus at the first follow-up visit and has remained so to the present.

DISCUSSION

Ectopia of the ureteral orifice results from the failure of craniolateral shifting of the ureter, as the wolffian duct, from which the ureter springs by budding, migrates downward and medially to form the seminal tract and posterior urethra. Where craniolateral shifting of the ureter does not occur, it is carried downward with the wolffian duct resulting in its opening into a wolffian duct derivative—the posterior urethra, seminal vesicle, ejaculatory duct or vas deferens in the male; and in the urethra, vestible or Gaertner's duct in the female. Those cases in which the ureter opens into derivatives of the müllerian duct such as the utricle in the male and the uterus or fallopian tubes in the female are difficult to explain embryologically. Other congenital genito-urinary abnormalities, though not involved in the mechanisms resulting in ureteral ectopia, are fairly common in these patients.

The usual clinical history obtained from females with ureteral ectopia is that of diurnal and nocturnal incontinence independent of regular and normal bladder function. Incontinence is not present in the male since the opening is proximal to the external sphincter. The clinical picture in the male is usually that of a complicating infection and the diagnosis is more difficult.

SUMMARY AND CONCLUSIONS

A case of ureteral ectopia associated with renal dystopia in a male child is presented. The only complaint was pyuria of long duration.

This case emphasizes the importance of thorough urological study of children with persistent pyuria. It also emphasizes the importance of considering the presence of an ectopic ureteral orifice where one fails to find a ureteral orifice in its usual site.

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REFERENCES

ABESHOUSE, B. E., GOLDSTEIN, A. E. AND TANKIN, L. H.: Ectopic ureteral orifice; a report of four cases. Urol. and Cutan. Rev., **54**: 7, 1950.

BURFORD, C. E., GLENN, J. E. AND BURFORD, E. H.: Ureteral ectopia: A review of the literature and two case reports. J. Urol., **63**: 211, 1949.

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PRIMARY AMYLOID TUMOR OF THE BLADDER: REPORT OF A CASE

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The subject of primary amyloid tumors of the bladder has recently been reviewed by Craig. He was able to find 7 cases reported in the literature, and added an eighth case, unique in that it was the first instance treated by transurethral electrocoagulation. Craig's case showed no evidence of recurrence after 6 years.

In his patient, as well as in only one other reported case, the diagnosis was made by cystoscopic biopsy, while in the remainder of the reported cases, diagnosis was made either on surgical excision or autopsy. In none of the cases was the true nature of the lesion suspected prior to pathological examination; the clinical suspicion of neoplasm arose instead. This same pattern was followed in our own patient: the clinical impression was that of malignant infiltrating tumor and the exact diagnosis was made only by microscopic examination after transurethral resection.

In all of the reported cases, as well as our own, the outstanding presenting symptom was gross profuse hematuria. It is this characteristic of bleeding which has caused considerable difficulty in the surgical handling of the lesion. In none of the reported cases, partly because of this feature of bleeding, and partly because of the clinical impression of malignant tumor, has the surgical approach been that of transurethral resection of the tumor, although Craig reported that he treated his patient by electrocoagulation of the lesion through the cystoscope.

The following case is presented as the ninth reported in the literature, of the problem of primary amyloid tumor of the bladder. Of all of the reviewed cases, this is the only one which has been treated by transurethral resection, apparently successfully. Although the period of follow-up is limited, there has been no evidence of recurrence in 22 months.

It must be emphasized that this is a case of primary solitary amyloid tumor; such an entity must be distinguished from secondary generalized amyloidosis, the result either of a chronic suppurative process or the concomitant of multiple myeloma. Our patient showed no clinical evidences of any such disease, nor were any other amyloid deposits to be found elsewhere after specific search for such dissemination.

CASE REPORT

A 55 year old, married, white man was first seen on July 13, 1949, because of hematuria which had begun 4 days prior to office visit and had continued since then. The hematuria was entirely painless. The blood was evenly distributed throughout the urine with no clots present although it was quite profuse. No history of nocturia, frequency or dysuria was obtained. There were no episodes of prior urinary symptoms, although terminal hematuria had occurred on one occasion approximately two years previously. As this did not recur, a physician was not consulted. Previous surgery was limited to appendectomy and later repair of an incisional hernia. Office cystoscopy disclosed the presence of a bladder tumor, and the patient was referred to the hospital.

He was admitted to the hospital July 14, 1949. Physical examination was essentially negative. On rectal examination, the prostate was recorded as "slightly enlarged." The blood pressure was 110/74. The blood count revealed 4,520,000 erythrocytes; 14 grams of hemoglobin; 6,500 leukocytes with 54 per cent neutrophiles, 1 per cent basophiles, 1 per cent eosinophils, 40 per cent lymphocytes, and 4 per cent monocytes. The urinalysis, on grossly bloody urine, was reported as: Specific gravity 1.026; reaction, acid; protein, 2 plus; acetone, very faint trace; diacetic acid, negative; many red blood cells and 10-12 white blood cells per high power field (centrifuged). The serological tests for syphilis were negative. Blood urea nitrogen was 16 mg. per cent, and blood glucose was 70 mg. per cent. Excretory urography disclosed a normal upper urinary tract.

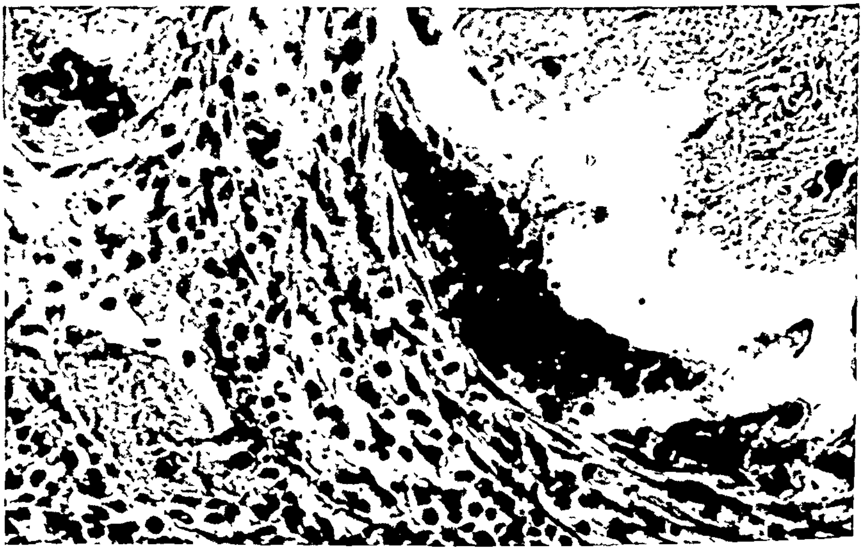

FIG. 1. Section from portion of tumor removed (×100). Amorphous, rather homogeneous material in upper half of section is amyloid.

On July 15, cystoscopic examination was done under spinal anesthesia. Inspection revealed a flat, infiltrating irregular mass extending obliquely across the trigone to the vesical neck. The left ureteral orifice was obscured by the mass, and the right was partially surrounded but could be identified. The tumor was yellowish-red in color and seemed to be invasive. Elsewhere the bladder appeared normal. A tentative diagnosis of malignant neoplasm was made. Bimanual examination showed no apparent spread outside the bladder.

A 28F Stern-McCarthy resectoscope was substituted for the cystoscope. The original intention had been to obtain a biopsy, but, as bleeding was minimal, all tumor tissue seen was resected down to and including part of the bladder muscle. Both ureteral orifices were visible at the end of resection. Bleeding was well controlled by electrocoagulation; a 22F Foley catheter was inserted, and 10,000 units of topical thrombin was instilled into the bladder.

The microscopic examination (fig. 1) was reported by Dr. S. Gross: "Sections through the bladder reveal the epithelium to be intact in most areas. Occasionally small nests of epithelium are seen in the lamina propria. The latter is diffusely infiltrated by lymphocytes and plasma cells. In addition, in the lamina propria and muscularis there are small and larger collections of amorphous eosinophilic material. The material appears to replace muscle bundles and fibers in scattered areas. Occasional clumps of this material are noted. These are surrounded by an inflammatory reaction, including numerous lymphocytes and multinucleated foreign body type giant cells. Similar eosinophilic material thickens the walls of some blood vessels.

"With special stain (crystal violet) this material stains like amyloid."

"No neoplasm is seen in any of the many sections taken."

"Diagnosis: Amyloidosis of urinary bladder."

The patient received penicillin and sulfadiazine postoperatively. He was afebrile during his hospital stay. The urine was quite clear on July 17, two days following resection, at which time the indwelling catheter was removed. Voiding was spontaneous and the urine remained clear. On the fourth postoperative day (July 19) the patient was dismissed from the hospital.

Follow-up has been continued at the office. Cystoscopy as late as May 1951 (twenty-two months postoperatively), revealed no evidence of recurrence. Blood protein determinations done December 21, 1949 were: Total, 6.4 gm. per cent; albumin 4.2; globulin 2.2; A/G ratio 1.9. To date, the patient remains free of urinary symptoms and urinalysis is negative.

SUMMARY

The ninth reported case of primary amyloid tumor of the bladder has been presented. Though the lesion is rare, it is of considerable clinical interest because it is similar to and is mistaken for an invading malignant neoplasm of the bladder. The distinction between the two lesions, which can only be made on pathologic microscopic examination, must be made because primary amyloid tumor is evidently a nonrecurrent benign problem. The outstanding clinical symptom of vesical amyloidosis is hematuria.

This is the first reported case treated by transurethral resection.

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REFERENCES

CRAIG, L. G.: Amyloid tumor of the bladder. J. Urol., **61**: 365, 1949.

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PROSTATIC CARCINOMA WITH METASTASIS TO THE TESTICLE

ALLEN C. BRADHAM

Since the report of Semans of the first case of carcinoma of the prostate with metastasis to the testicle, 2 additional similar cases have been reported. It is my desire to add the fourth case to the literature, none of which have been diagnosed clinically prior to operation or autopsy.

CASE REPORT

A. B. H. Sr. (Hosp. No. 17) was referred to the author on January 1, 1949 with a chief complaint of "leakage of urine." He stated that for a year or more he had been unable to urinate without a concurrent bowel movement and suffered from almost continuous leakage of his urine. On occasion he had passed some bloody urine. He had never been catheterized. Because of a chronically distended bladder, he suffered much pain and discomfort from distention but denied any undue backache. His general health had been good and, in spite of his urinary discomfort, he had managed to do a limited amount of farm work. His past history was negative for surgery or serious illness.

Physical examination revealed a tall, slender 74 year old white man, alert, and in no acute distress. A review of systems revealed negative findings with the exception of a generalized arteriosclerosis and the genito-urinary findings to follow. His blood pressure reading was systolic 156, disatolic 76 mm. mercury and hemoglobin 64 per cent Sahli. Neither kidney was palpable nor tender. The right scrotal contents revealed a knotty mass apparently above the right testicle which resembled varicosities; it was not tender or fluctuant with no apparent involvement of the vas deferens or associated structures. The patient stated this mass had been present for several years and had never increased in size nor caused any discomfort. The left scrotal contents were normal. The penis appeared normal and the urethra calibrated to normal size. On rectal palpation, a huge prostate seemed to fill the entire rectum; it was soft, fluctuant, and free of nodules suggestive of malignancy. He could pass only a few cubic centimeters of urine so a 12F Tieman catheter was passed to the bladder and 48 ounces retained urine evacuated. Urinalysis revealed a hazy, yellow specimen of acid reaction, (pH 5.0) specific gravity 1:008; albumin negative; sugar negative; rare pus cell and 8–10 blood cells per high power field.

An attempt was made to introduce a 16F Brown-Buerger observation cystoscope which was unsuccessful. An 18F Foley catheter was fixed in the bladder and the patient admitted to the Anderson Memorial Hospital the same day. The following data were obtained at the hospital: total erythrocyte count 4,100,000; leukocyte count 8,200; hemoglobin 80 per cent; polymorphonuclears 69 per cent; lymphocytes 26 per cent; eosinophils 5 per cent. The blood urea nitrogen recorded 35 mg. per 100 cc and the blood Kline was negative. A 2 hour phenolsulfonphthalein test done the following day excreted 18.5 per cent at the first and

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Read at annual meeting, Southeastern Section, American Urological Association, Gulfport, Miss., February 3, 1950.

second hours for a total output of 37 per cent. X-rays of spine, ilia and femora were all negative for evidence of bony metastasis although malignancy was not suspected and this was done on a purely routine basis. An excretory urogram revealed fair excretion of the dye in each kidney within 5 minutes after administration with essentially normal appearing calyces, pelves, and ureters.

On January 5, 1949 a one-stage suprapubic prostatectomy was done under pontocaine spinal anesthesia supplemented by pentothal sodium intravenously. Through a Pfannenstiel incision, the urinary bladder was opened whereupon a large protrusion was noted into the vesical cavity. The mucosa was acutely reddened and grossly trabeculated. On enucleation of the prostate, it was noted that the lateral lobes were fibrous and firm in consistency while the posterior lobe crumbled into a jelly-like mass and it was necessary to scrape out this tissue with the enucleating fingers. The prostatic fossa was drained with a 26F Foley catheter introduced through the urethra and the bladder was closed around a 24F Foley catheter brought out through the suprapubic wound.

In response to antibiotics, sulfonamides, fluids, blood transfusions, the patient had a rather smooth convalescence and the suprapubic wound healed rapidly. It was a total surprise to encounter this type of tissue at operation and malignancy was suspected for the first time. The following pathological report confirmed our opinion:—

The specimen consisted of one large, firm but compressible, enucleated piece of prostate measuring 4.5 by 5 by 4.5 cm. The cut surface of this mass was grey to grey yellow. Also included were numerous pieces of prostatic tissue which resemble those removed by transurethral resection together with blood clots weighing 40 gm. The entire specimen weighed 75 gm.

Microscopic: Sections from the large piece of prostate tissue were composed mainly of tumor cells. The tumor cells were arranged in definite but irregular acinar structures in some areas but, for the most part, they replaced the fibromuscular stroma and showed little tendency to form acini. They infiltrated the stroma diffusely as small, closely packed strands. The individual tumor cells were columnar with pale, clear refractile cytoplasm, and rounded vesicular nuclei, with only a few mitoses. In the areas diffusely infiltrated by tumor cells, the nuclei were more irregular, showed frequent mitoses and the cytoplasm more refractile. There were a few areas showing hypertrophic type prostatic glands containing some secretion material. Perineural invasion by tumor cells was not observed. Sections of the smaller prostatic chips showed complete replacement of the stroma by tumors similar to the diffusely infiltrated areas described above. Diagnosis: adenocarcinoma of the prostate, diffuse and papillary type (fig. 1).

Upon receipt of the pathological confirmation, our attention was then focused on the lesion in the right scrotum. A bilateral orchiectomy was done January 14 under pentothal anesthesia. On opening the right scrotum, the testicle was found to be indurated containing multiple cystlike structures filled with clear fluid. The overlying veins were dilated and prominent which confirmed the suspicion of malignancy. The left testicle was normal.

Specimens were submitted for pathological study and it is regretted that a photograph was not made of the gross specimens. The specimen consisted of one oval shaped testicle showing a tear in the capsule. The testicle measured 5 by 4 by 3.5 cm. On section, the surface was homogeneous, tan in color, soft in consistency and bulging. The substance was very friable and was composed of irregular, papillary like tumor tissue. The epididymis was not recognized.

Microscopic: The capsule of the testicle was intact in one area but showed extreme edema and infiltration of lymphocytes. Beneath this capsule the seminiferous tubules showed extreme atrophy. The adjoining tissue was composed of irregular, papillary shaped structures covered with tall columnar epithelium containing a clear, refractile, vaculated cytoplasm and a small dark round vesicular nucleus. The nuclei were fairly uniform in size and shape. Scattered mitoses were seen throughout the tumor. The stroma was very scant and contained no lymphocytes. Approximately 95 per cent of the parenchyma of the testicle was replaced by tumor tissue. Permeation of the endothelial lined spaces by tumor cells was observed in the rete testis region.

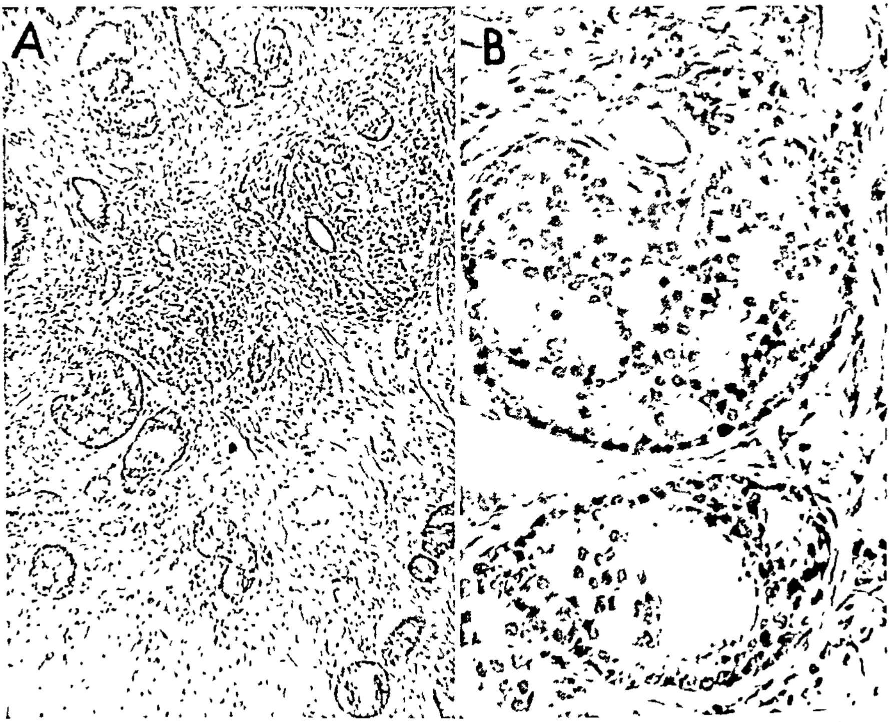

FIG. 1. Low and high power photomicrographs of adenocarcinoma of prostate

The same cell types appeared in both the prostate and testicle of the patient, except that the papillary pattern was more pronounced in the secondary tumor of the testicle. The prognosis was considered grave because of the likelihood of distant metastases. Diagnosis: Metastatic adenocarcinoma of testicle from prostate (fig. 2).

On January 22 a chest x-ray was negative for metastatic lesions. The patient made an uneventful recovery and was discharged from the hospital on the twenty-sixth postoperative day. He was urinating without difficulty and was instructed to take diethylstibestrol 5 mg. daily until further notified.

The patient lived in a distant town and it has been difficult to follow him as closely as desired. He returned to the office on May 5 at which time he stated he had been working every day on his farm and he had gained 11 pounds in weight. He complained of slight sphincter weakness when up on his feet but nocturia only 1–2 times. Voided urine showed a trace of albumin, 8–10 blood cells and an occasional pus cell in each high dry field. His residual urine measured ½ ounce (15 cc) and the operative scars appeared healthy. The bladder capacity exceeded 8 ounces (240 cc) and he appeared to have good urinary control. He was requested to return at an early date which he has failed to do.

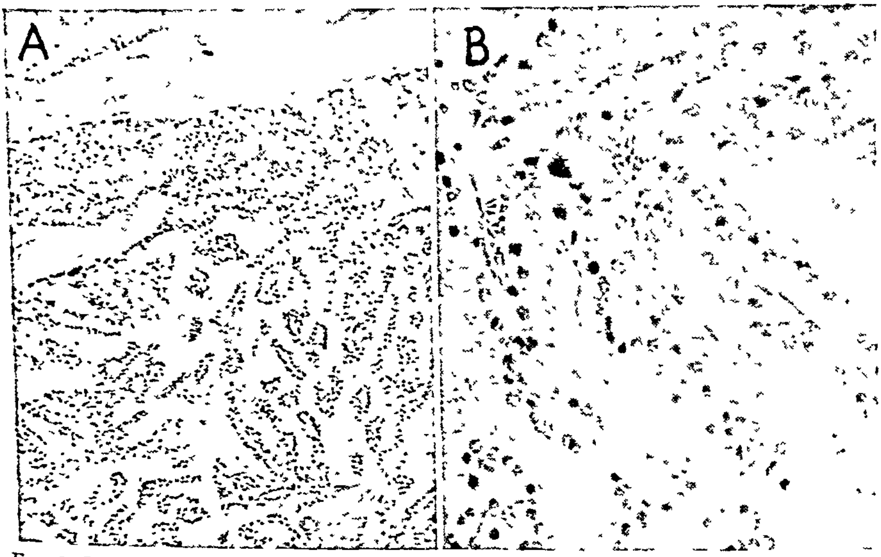

FIG. 2. Low and high power of adenocarcinoma of testicle metastatic from prostate

Because of the rarity of this condition, our pathologist, Dr. D. F. Mullins, Jr. of Athens, Ga. referred slides of the sections to Col. J. E. Ash of the Army Medical Museum for study and I quote his comments: "I have been puzzling over the slides in the case of Mr. H x-49-3029 and x-49-3131, and while they are interesting, they are a bit difficult to interpret. I don't remember having seen this particular combination before. I do know, however, that both tumors are the same and, judging from the pictures in the two organs, I would pick the prostate, as you have, as the site of the primary tumor. The bulk of the tumor is surprisingly well differentiated, particularly in the testicular mass, but there is ample evidence in the prostate of frank malignancy. It would be surprising if he did not have metastasis elsewhere."

DISCUSSION

Helfert and Pinck, in reporting the second case of prostatic carcinoma with metastasis to the testicle in 1944, made the statement that metastatic tumors to the testicle from all sources are exceedingly rare. A survey of the literature at that time revealed less than fifty such cases. Semans listed the following sites for prostatic metastasis in carcinoma in 140 cases studied at the Johns Hopkins Hospital in 1938: 1) pelvic lymph nodes in 43 cases; 2) urinary bladder in 31 cases; 3) seminal vesicles in 21 cases; 4) rectum in 8 cases; 5) lungs in 26 cases; 6) osseous system in 18 cases; 7) retroperitoneal, mediastinal and bronchial lymph nodes in 16 cases; 8) liver in 12 cases; 9) ureter in 7 cases; 10) pleura in 5 cases; 11) adrenal glands in 5 cases; 12) diaphragm in 4 cases; 13) peritoneum in 3 cases; 14) pancreas in 2 cases; the vas deferens, urethra, and kidneys were each involved once.

All the three previously reported cases have shown the presence of metastatic lesions in areas other than in the testicles. In the case reported by Semans, autopsy revealed metastasis to the sacrum and lumbar vertebrae. The case of Helfert and Pinck showed osseous lesions in the skull, lumbar vertebrae, pelvic bones, and upper femora as determined by x-rays. On follow-up x-rays, the case reported by Baird and Hare revealed metastatic lesions in the ribs, pelvis, and left femur. To date, there has been no evidence by clinical examination or x-ray of metastasis other than to the right testicle. It is quite possible that additional sites will be revealed on later studies.

The authors of the 3 previously reported cases all agree that in each single case, metastasis occurred by arterial extension or embolism. Helfert and Pinck reached this conclusion on the reasons that it is the most common route and the presence of widespread osseous extension which bore out a prerequisite of arterial extension. In this fourth case, arterial embolus was searched for and not found, bony and pulmonary metastases were not demonstrable, and considerable tumor tissue was demonstrated in the veins and tubules of the testicle and epididymis. It would appear doubtful, then, that metastasis occurred by the arterial route. The three modes of extension are 1) retrograde venous extension or embolism; 2) retrograde lymphatic extension; 3) arterial embolism. Secondary involvement of the testicle by retrograde lymphatic extension is also uncommon.

SUMMARY

The fourth case of carcinoma of the prostate with metastasis to the testicle is herewith added to the literature. No case has been diagnosed clinically prior to surgery or autopsy.

Grateful acknowledgement for his valuable pathological studies, slides, and microphotographs is herewith made to Dr. D. F. Mullins, Jr., pathologist to St. Mary's Hospital, Athens, Ga. I wish to thank Col. J. E. Ash of the Army Medical Museum for his valuable criticisms and opinions of the slides studied.

Anderson, S. C.

REFERENCES

Baird, S. S. and Hare, D. M.: J. Urol., **59:** 1208–1211, 1948.
Helfert, I. and Pinck, B. M.: J. Urol., **51:** 635–640, 1944.
Semans, J. H.: J. Urol., **40:** 524–529, 1938.

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GENITO-URINARY TRACT INFECTIONS: EXPERIENCES WITH IN VITRO SENSITIVITY TESTS IN CHOICE OF ANTIBIOTICS

JOSEPH C. HAYWARD, JAMES B. GLANTON AND LOUIS M. ORR

It is the intent of our rather cursory investigation to present a method whereby a more accurate approach to the problem of control and eradication of bacteria in the urinary system can be realized. Up to twenty-five years ago efforts to combat infections in this part of the body were for the most part quite futile. In recent years, however, and almost within months, the tremendous strides in the development of antibiotics have been little short of miraculous.

The difficulties which have been experienced in clearing up such pathological changes are apparent in view of the many medications and other therapeutic measures which have been tried with varying degrees of success. The organisms usually encountered can be identified, as extensive investigation has been carried on in this field during recent years. See figure 1.

When penicillin, shortly after its discovery by Sir Alexander Fleming, was enjoying greatest publicity and cure-all claims, one of our colleagues at the American Urological Association meeting in St. Louis in 1944 gave a brief discussion of the gonococcus versus penicillin. Numerous essays had just been read describing the dosages of penicillin proved necessary to clear up even the most resistant cases of gonorrhea, when the discussant briefly reviewed the history of the gonococcus, starting from the time of Moses and the children of Israel, passing on through the other various medications; viz., silver instillations, sounds, mercurochrome, hyperpyrexia, sulfonomides, and finally the death note for the "coffee-bean" organism, penicillin. It was his belief that in spite of all the scientific data suggestive of complete eradication of gonorrhea, one could still place his money on the gonococcus. Time has proven him to be right.

Further research has developed streptomycin, which has proven to be of great value. However, a need for more powerful medications has led to the development of perhaps the most effective antibiotics for genito-urinary infections, aureomycin and chloromycetin. It is well for us to recognize that during the past few years the various organisms which are responsible for most infections of the urinary tract have encountered new therapeutic measures which have by this time destroyed all but the hardiest and most resistant. Usually by the time a patient is seen in a urologist's office because of urinary tract infection, he has been treated by one or more general practitioners who have tried several antibiotics without success.

Regardless of the careful selection of a proper antibiotic, its use will prove ineffective in the face of stasis or other surgical pathology. If a patient is to receive adequate care, it is necessary that an accurate determination of the causative organism be made. Urinary or prostatic cultures are simple to obtain and it has been our experience that in vitro sensitivity tests to determine the most effective antibiotic have proven most valuable. To determine the most

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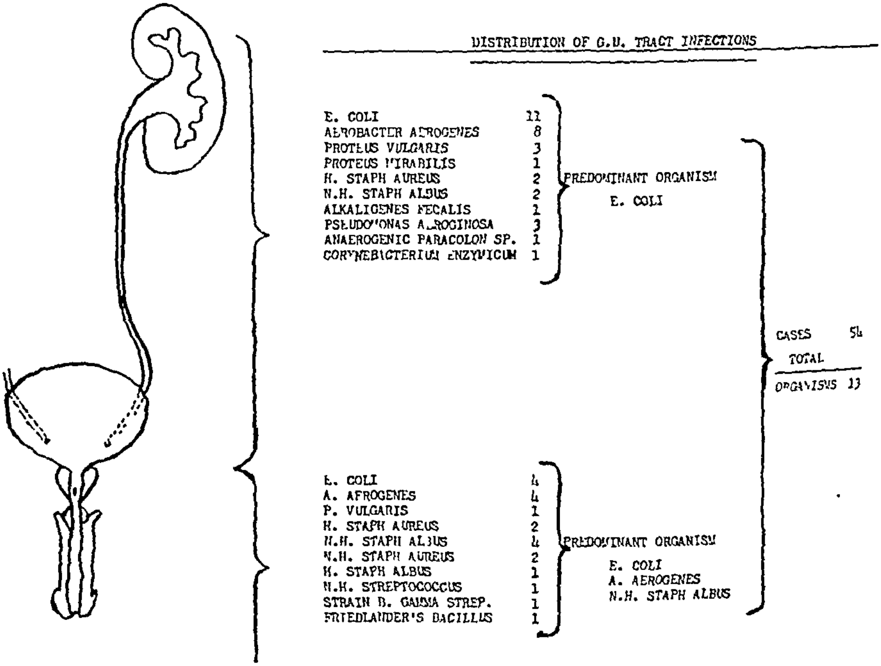
Read at annual meeting, Southeastern Section, American Urological Association, Gulfport, Miss., February 4, 1950.

effective antibiotic in any given infection, we wish to present a practical plan applicable to every day office procedure, and to state the clinical, not laboratory, results following the use of this method in the selection of antibiotics.

The method of testing organisms for in vitro sensitivity to antibiotics is one that can easily be accomplished in the ordinary hospital laboratory. The exact procedure used is as follows:

METHOD OF TESTING ORGANISMS FOR IN VITRO SENSITIVITY TO ANTIBIOTICS

Immediately prior to starting the test the following materials are prepared and kept in readiness.



DISTRIBUTION OF G.U. TRACT INFECTIONS

E. COLI	11
AEROBACTER AEROGENES	8
PROTEUS VULGARIS	3
PROTEUS MIRABILIS	1
H. STAPH AUREUS	2
N.H. STAPH ALBUS	2
ALKALIGENES FECALIS	1
PSEUDOMONAS AEROGINOSA	3
ANAEROGENIC PARACOLON SP.	1
CORYNEBACTERIUM ENZYMICUM	1

PREDOMINANT ORGANISM
E. COLI

CASES 54
TOTAL
ORGANISMS 13

E. COLI	4
A. AEROGENES	4
P. VULGARIS	1
H. STAPH AUREUS	2
N.H. STAPH ALBUS	4
N.H. STAPH AUREUS	2
H. STAPH ALBUS	1
N.H. STREPTOCOCCUS	1
STRAIN B. GAMMA STREP.	1
FRIEDLANDER'S BACILLUS	1

PREDOMINANT ORGANISM
E. COLI
A. AEROGENES
N.H. STAPH ALBUS

FIG. 1

1. Sufficient number of sterile Petri dishes, one for each drug to be tested.
2. Supply of antibiotics on which sensitivity tests are desired.
3. Sterile distilled water.
4. A supply of sterile filter paper discs approximately 1 cm. in diameter. These may be cut from ordinary filter paper with a cork borer and kept sterile in a Petri dish. Any smooth surface filter paper is satisfactory. Whatmans No. 2 has been found quite suitable.
5. Several flasks of freshly prepared culture media suitable for growing the organism under test, about 25 mm. for each plate.
6. Vigorous growing, approximately 18 hour old, broth culture of the organism to be tested.

Method of procedure. The flask of agar is melted and allowed to cool to approximately 45 degrees centigrade and this agar is seeded with 2 or 3 cc of young, vigorously growing broth culture of the organism to be tested. Care must be exercised that the agar is not sufficiently hot to sterilize the culture, otherwise no growth will be obtained. The culture is mixed with the agar by slowly rotating the flask. Care should be exercised that the flask is not shaken vigorously so as to incorporate air bubbles into the medium. A sufficient number of Petri dishes to accommodate the drugs to be tested, one plate for each drug, are poured from the seeded agar mixture and allowed to harden. Before the agar has hardened, carefully flame the surface of each Petri dish with a Bunsen burner to break up any air bubbles which might appear on the surface. It is important that the surface of the agar be perfectly smooth and there be no pits or air bubbles. The lids of the Petri dishes are allowed to remain slightly ajar in order that there be as little water of condensation as possible on the plates. A fairly dry surface to the plate is quite important.

After the plates have hardened, place in the center of each a circle of sterilized filter paper and carefully press in intimate contact with the agar by means of a flattened glass rod or end of a test tube. In the center of each filter paper disc place 5 mg. of the antibiotic to be tested. Special care must be exercised that all of the antibiotic is placed on the filter paper and none is allowed to sift onto the surface of the medium. After the antibiotics have been placed in the center of the filter paper discs, carefully place on each a small drop of sterile distilled water. It is especially important that the drop of water be of such size that the filter paper is entirely moistened, but not sufficiently large that any of the water will creep off on the surface of the medium or remain unabsorbed on the filter paper. The filter paper must be moist but not flooded with water. The selection of a proper size dropper requires some experience and experiment, but is very easily accomplished by trial and error.

The Petri dishes are then covered, inverted, and placed in the incubator for 24 to 48 hours, depending on the rate of growth of the organism under test. At the end of the incubation period they are removed and the zone of inhibition surrounding the filter paper disc is read. If there is no clear zone surrounding the filter paper disc showing that there has been no inhibition of growth by the antibiotic, the test is read as "no inhibition." If there is a very narrow, hazy margin showing that there is only partial or indefinite amount of inhibition, the test is read as "plus-minus." Clear zones of inhibition up to 0.5 cm. are read as "1 plus inhibition." Clear zones of inhibition up to 1 cm. are read as "2 plus inhibition." Clear zones of 1 to 1.5 cm. are read as "3 plus inhibition." All zones of definite inhibition over 2 cm. beyond the edge of the filter paper are read as "4 plus inhibition." See figure 2.

It is advisable to run at the same time a control on the growth of the organism without any antibiotic. It is also advisable to test selected strains of an organism whose sensitivity is known. Such strains of organisms can be obtained from the national type culture collection at Georgetown University.*

By using the method presented, we have found it easy to identify the etiological organism and give a relatively accurate index as to the antibiotic which will prove most effective in eradicating the infection. Negative findings are most valuable, in that oftentimes it is learned that one or possibly three of the agents being tested will exhibit no inhibition on the growth of the organism in question. It is therefore apparent that to prescribe these expensive agents would be unwarranted. Complete cultures with in vitro sensitivity tests are sometimes regarded as an unnecessary expense; however, it is our belief that most of the time these studies will in reality be a real saving to the patient, as well as shortening the illness.

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* Herring's Laboratory Procedure, Orlando, Florida

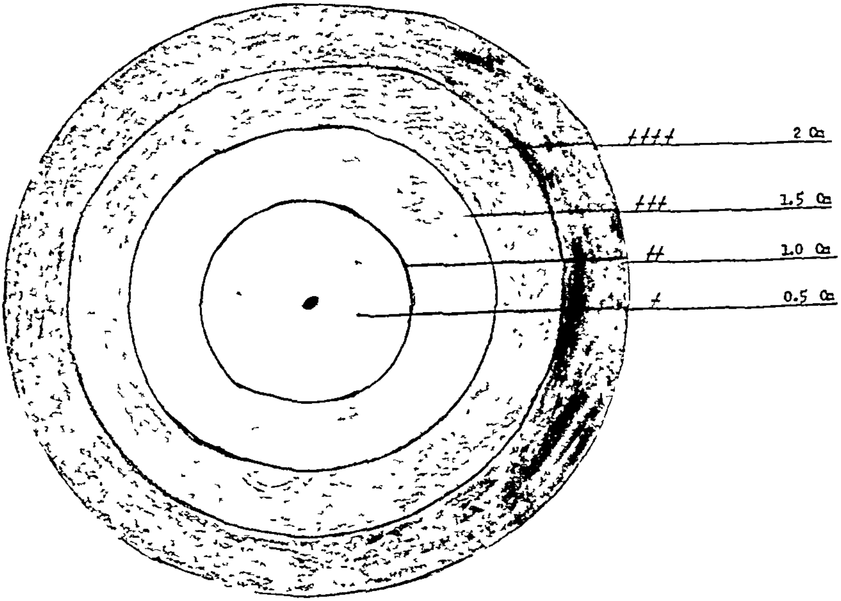

FIG. 2 Degrees of inhibition exhibited by specific antibiotics against various organisms.

While preparing this report, we were most interested to learn that on one occasion complete study was made of the organism and its sensitivity to medications, which revealed that all but one of the products being studied produced no inhibition and the other gave complete inhibition in dilute concentration. In checking over the clinical results, it was observed that the patient in question had received a drug which had not been included in our sensitivity tests. Apparently the laboratory report had been returned to us, attached to the patient's record and the results never correlated, much to our chagrin. A definite system for follow-through application of the results is necessary if similar mistakes are to be avoided.

These studies have helped us to more promptly and adequately treat patients with genito-urinary tract infections with most encouraging objective and subjective benefits to the patient. Follow-up cultures have not been routinely accomplished, as these patients primarily represent private office practice and circumstances have not permitted what would be ideal follow-up investigations for obvious economic reasons.

CONCLUSION

Cultures with in vitro sensitivity tests on specimens obtained from the genito-urinary tract have proved an effective adjunct in the management of infections, particularly those of a chronic nature. This regimen has economical recommendations for its use in that trial and error use of expensive antibiotics is thus eliminated. A practical method for conducting the recommended investigations has been presented.

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EXTRA-URETHRAL CONFINES OF URETHROGRAPHIC CONTRAST MEDIUM

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Urethrography as a method of diagnosis of lower urinary tract disease is attended with the possibility of extravasation or invasion of contrast media into areas outside the lumen proper of the male urethra. Innumerable urethrograms performed in the course of diagnostic study reveal the presence of contrast media in a variety of peri-urethral and remote locations. Intra-urethral injection of media other than urethrographic contrast media have been observed to trespass the boundaries of the male urethra. In 1931, Patterson reported 2 cases of fatal oil embolism following dilatation of urethral strictures with oil. Cyanosis, dyspnea and hemiplegia occurred immediately after injection, and death resulted within 15 minutes in 1 case and within 7 hours in the other. The sudden hemiplegia gave presumptive evidence of cerebral oil embolism. Post-mortem examination revealed that large amounts of oil were diffusely distributed throughout both lungs. In 1935, Carr and Johnson described a case of fat embolism following instrumentation and injection of oil into the urinary bladder. Death occurred within 4 hours. Oil was found in the lungs, kidneys and brain on post-mortem examination. In 1947, Crabtree found in the literature 27 cases of venous invasion following urethrography and 4 fatalities due to fat emboli following the intra-urethral injection of oily urethrographic contrast media. In 1949, Gaudin described a case of fatal coronary embolism from the use of barium for urethrography which he performed with the same medium in some hundreds of cases over a 5-year period.

The oily content of contrast media has also been cited as the incriminating factor in the production of serious untoward reactions during the roentgenological study of the female genital tract as revealed by the record of fatalities following hystero-salpingography. Martland disclosed that fat or oil embolism has been observed in criminal abortion following the use of soapy soutions which after injection into the uterine cavity gain access to open uterine venous sinuses upon separation of the placenta.

The pathogenesis of extra-urethral invasion of urethrographic contrast medium implicates several important factors, namely, the integrity of the urethra, the vascularity of urethral confines, the nature of the contrast medium used relative to oily content and viscosity, the quantity of medium delivered to extraneous foci, the rate of injection and the degree of pressure utilized during the performance of urethrography.

The purpose of this study is to correlate some of the varieties of extra-urethral

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Read at meeting of New York Society, American Urological Association, Yale Club, April 19, 1950.

Note by editor. Dr. Fernicola's paper was selected by the Award Committee of the New York Society as the Prize Essay Award for 1950. The prize is offered annually to the intern and resident staffs of hospitals within the area of the New York Society.

configurations of urethrographic contrast medium with urethral disease entities and to determine the relative influence of the various factors instrumental in the production of extravasation or intravasation of urethrographic contrast medium.

Two hundred urethrograms were done on males with suspected or demonstrable lower urinary tract disease including urethral stricture, congenital, acquired and spasmodic, urethral fistulas, urethral tumor, urethral injury, urethral calculi, urethral diverticula, urethritis, peri-urethral phlegmon, hyperplasia and carcinoma of the prostate, prostatic abscess, prostatic calculosis and chronic prostatitis. Hematuria was present in 12 cases, 7 of which had urethral bleeding. The youngest patient was 14 years and the oldest 91 years.

The significant results of this study were the high percentage of some degree of invasion of extra-urethral anatomical confines, the absence of untoward effects, the observation that urethrographic contrast medium was not extravasated from the normal urethra in the presence of excessive pressure and the fact that extensive venous invasion present in 4 instances occurred in the absence of excessive pressure or hematuria.

METHOD

This series of urethrograms was done with the Brodny urethrographic clamp and 30 cc B-D Yale syringe. The contrast medium used was iodochloral (Searle) which contains 27 per cent of iodine and 7.5 per cent of chlorine in organic combination with a highly refined peanut oil. Sterile mineral oil, 10 cc, was added to 20 cc of the iodochloral to make up 30 cc of solution for each urethrogram. Twenty-five cubic centimeters of solution was injected in the antero-posterior view, and the remaining 5 cc in the oblique view. A constant rate of injection of about 10 cc per minute was used, and exposures were taken during injection. Each urethrogram was done by the author whose subjective interpretation of the degree of manual pressure on the plunger of the syringe was recorded as slight pressure, moderate pressure, and excessive pressure.

Excessive pressure was used in no case with demonstrable or suspected urethral disease or hematuria. Slight or moderate pressure was recorded in all cases except in that of spasmodic stricture in which excessive pressure was used, and in which previous endoscopy revealed no organic urethral disease.

CLASSIFICATION

A classification of extra-urethral confines of urethrographic contrast media is proposed, and a tabulation of results is recorded (table 1).

VENOUS INVASION IN URETHROGRAPHY

Venous invasion in urethrography occasions greatest concern particularly when an oily contrast medium is used. The urethrographic medium enters the venous channels in the region of the anterior or posterior urethra and follows the branches of either the internal pudendal veins or inferior vesical veins, all of which empty into the hypogastric veins. The common iliac veins and inferior vena cava then provide pathways for the mechanism of pulmonary embolism or less often coronary, cerebral or general visceral embolism. Occasionally the deleterious circulating agent may have predilection for the vertebral venous system of Batson, by-pass the heart, and produce cerebral embolism. A patent foramen ovale, present in 25 per cent of individuals, according to Martland, may participate in the production of cerebral or visceral air emboli by shunting the pulmonary circulation and diverting the obnoxious agent into the left heart.

TABLE 1 *Extra-urethral confines of urethrographic contrast medium*

	NUMBER OF CASES	PERCENTAGE
Extra-urethral invasion	101	51
Urethrovascular injection	4	2
Urethroglandular invasion	49	24½
a Urethroprostatic reflux	26	13
b. Cowper's gland invasion	0	0
c Urethral gland invasion	23	11½
Urethral fistula	22	11
a. Urethrorectal fistula	0	0
b Urethroperineal fistula	20	10
c. Urethro-abdominal fistula	0	0
d. Fistula of the pendulous urethra	2	1
Urethro-interstitial invasion	19	9½
a. Prostatic abscess	3	1½
b. Rupture of the urethra	1	½
c Peri-urethral phlegmon	9	4½
d. Peri-urethral abscess	6	3
Urethral diverticula	9	4½
a. Congenital diverticulum	0	0
b Acquired diverticulum	9	4½
Anomalies	0	0

Total number of urethrograms performed 200

Several significant facts are illustrated in four instances of venous invasion (figs. 1, 2 and 3), and several pathogenetic considerations are suggested. In each of these cases chronic urethral disease existed in the nature of small caliber inflammatory strictures which led to occlusion of the urethra and to localized damage in mucosal, submucosal or corporal zones. The fragile epithelial lining of the male urethra is known by its behavior toward irritating solutions, instrumentation, trauma and infection. The delicate urethral epithelium in the presence of disease is not designed to endure the repeated strain of distention as is the epithelial lining of the urinary bladder, gallbladder or intestines. Columnar epithelium of which the urethral mucosa is composed is noteworthy in its inability to regenerate well anywhere in the body, and fibrous tissue response advances at a rate out of proportion to the inefficient cellular regeneration. The final condition of the urethra as a result of a variety of types of injury is an impairment to lesser or greater degree of the structural integrity of the urethra. Urethral disease is a prerequisite for the production of extra-urethral invasion

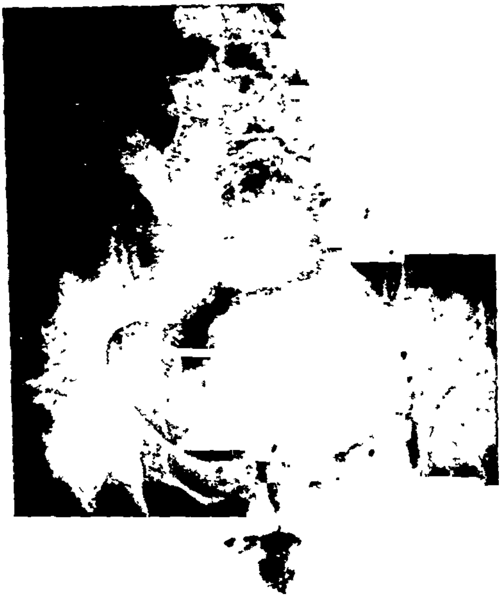

FIG. 1. Urethrovascular injection. Urethrogram shows contrast medium interrupted in its passage through bulbomembranous urethra. Extensive intravasation is visualized, and radiopaque oil globules present in branches of internal pudendal veins are seen extending upward into hypogastric and common iliac veins to inferior vena cava. Extreme local devitalization of tissue assuming form of acquired urethral diverticulum is seen in dilated, irregular portion of bulbous urethra. This case of venous invasion occurred under circumstances of slow injection, slight pressure and in absence of hematuria.

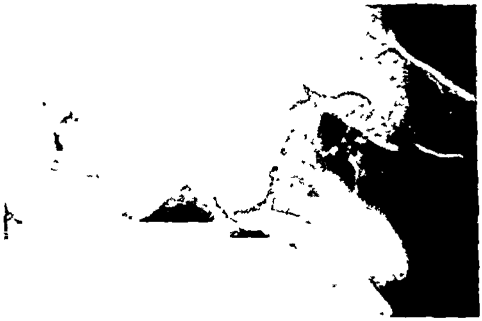

FIG. 2. Urethrovascular injection during state of erection of penis. Urethrogram shows extensive intravasation of entire venous system of erect penis. Circular branches of two deep dorsal veins which join as one deep dorsal vein at the root of penis, superficial dorsal vein and an upper scrotal vein are outlined A small caliber stricture in bulbous urethra and impassable stricture at bulbomembranous portion of urethra are seen. Extensive invasion of submucosal urethral glands is present in floor of pendulous urethra. This oblique view was taken during slow injection of remaining 5 cc urethrographic medium under slight pressure when erection of penis occurred.

of contrast media. That the effect of pressure or the rate of injection or the quantity of solution used can determine the degree of the final disposition of extravasated urethrographic media or that these factors may serve as immediate causes of extravasation is plausible, but neither of these factors is an underlying, required, causative element in the pathogenesis of extravasation or intravasation. A definite or potential break in the continuity of the mucosa in urethral disease offers ready access for a variety of agents to confines of the submucosa richly endowed with glands and vast anastomosing thin-walled venous plexuses. Since hematuria was not present in any of these cases of venous invasion it is reasonable to assume that a structural deficiency of the urethra, which is demonstrable urethrographically, and not an open venous sinus, provided entry of contrast medium into the mucosa to produce some degree of interstitial extravasation, microscopically minute as it may be. This interstitial harbor of medium in mucosal, submucosal or peri-urethral foci awaits the effect of secondary technical influences such as pressure, quantity of solution used and rate of injection to effect permeation of the thin-walled veins which in the presence of urethral disease have already participated in the infectious process. Localized thrombophlebitis and degeneration of the walls of the veins incurred as a result of infection enhance the possibility of vascular permeation of medium.

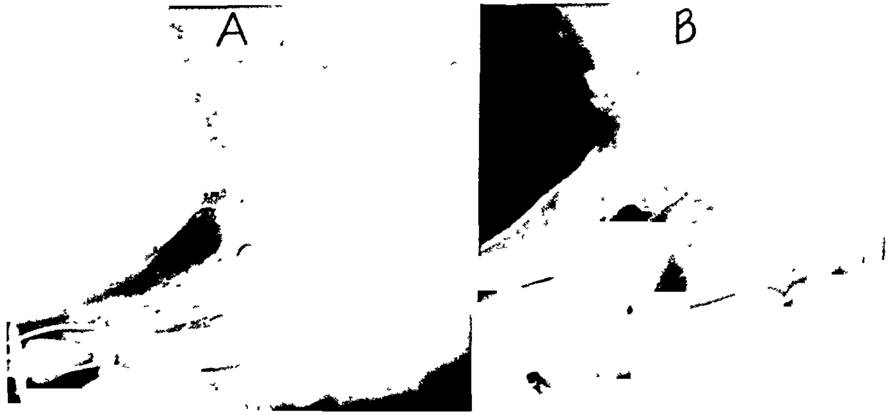

FIG. 3. *A*, urethrovascular injection. Urethrogram shows distended anterior urethra as a result of complete obstruction in bulbous urethra There is seen a marked invasion of tributaries of deep dorsal vein of penis and an outline of deep dorsal vein from glans to root of penis beneath symphysis pubis. *B*, urethrovascular injection. Urethrogram taken 2 days following urethrovascular injection seen in *A* reveals a repetition of invasion of deep dorsal vein of penis.

THE EFFECT OF PRESSURE IN URETHROGRAPHY

The effect of pressure during the performance of urethrography remains an important factor in the production of extravasation. There is shown, however, in the case of venous invasion of the erect penis that slight pressure is productive of intravasation while a subsequent urethrogram of the same case shows no extravasation with the use of greater pressure. It is demonstrated that excessive pressure will not induce extravasation of contrast medium in the normal urethra (fig. 4). At the same time it remains that urethral disease, particularly an occlusive disease of the urethra, is often the determining factor in the production of intra-urethral pressure in urethrography. This is especially the fact in urethral strictures, and the more occlusive stricture renders greater resistance to the flow of medium. More pressure is therefore required to propel the urethrographic medium beyond the obstruction. The presence of urethral disease remains as the underlying factor in the process. It is demonstrable that in the presence of a spasmodic stricture which permits little or no medium to enter the posterior urethra, and by virtue of a functional urethral obstruction producing excessive intraurethral pressure on injection of contrast medium, no extravasation occurs (fig. 5). The organically normal urethra does not permit invasion of its wall even in the presence of excessive pressure.

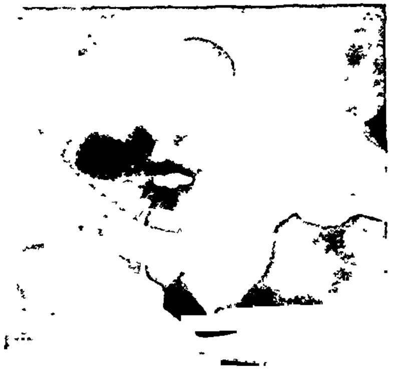

FIG. 4. Spasmodic stricture of urethra. Urethrogram done under excessive pressure reveals very small amount of contrast medium in posterior urethra and bladder as result of a spasmodic stricture of membranous urethra. Anterior urethra is shown to be distended to its limit, smooth and normal. No extravasation occurred in presence of excessive pressure.

THE FACTOR OF VASCULARITY IN THE PRODUCTION OF VENOUS INVASION

The factor of vascularity of the anatomical part participating in the process of venous invasion may be reasonably evaluated during the state of erection of the penis wherein a physiological increase of local blood volume is produced. It is difficult to ignore that the temporary state of increased blood volume of the penis influences the production of venous invasion (fig. 2). It is also reasonable to assume that in the presence of urethral disease and by virtue of an impassible urethral stricture against which the medium is injected, intra-urethral pressure of some degree is created. The acute passive congestion of the penile veins during the state of erection undoubtedly produces a local increase in venous pressure. The increased venous pressure provides a marked decrease in the rate of venous blood flow which enhances the degree of intravascular invasion of medium. The gaping and distended veins of the erectile penis make themselves readily accessible to the entry of contrast medium and divert the intravasation from branches of the internal pudendal or inferior vesical veins not partaking in the vascular process of erection of the penis. This divergence of venous invasion prevents the

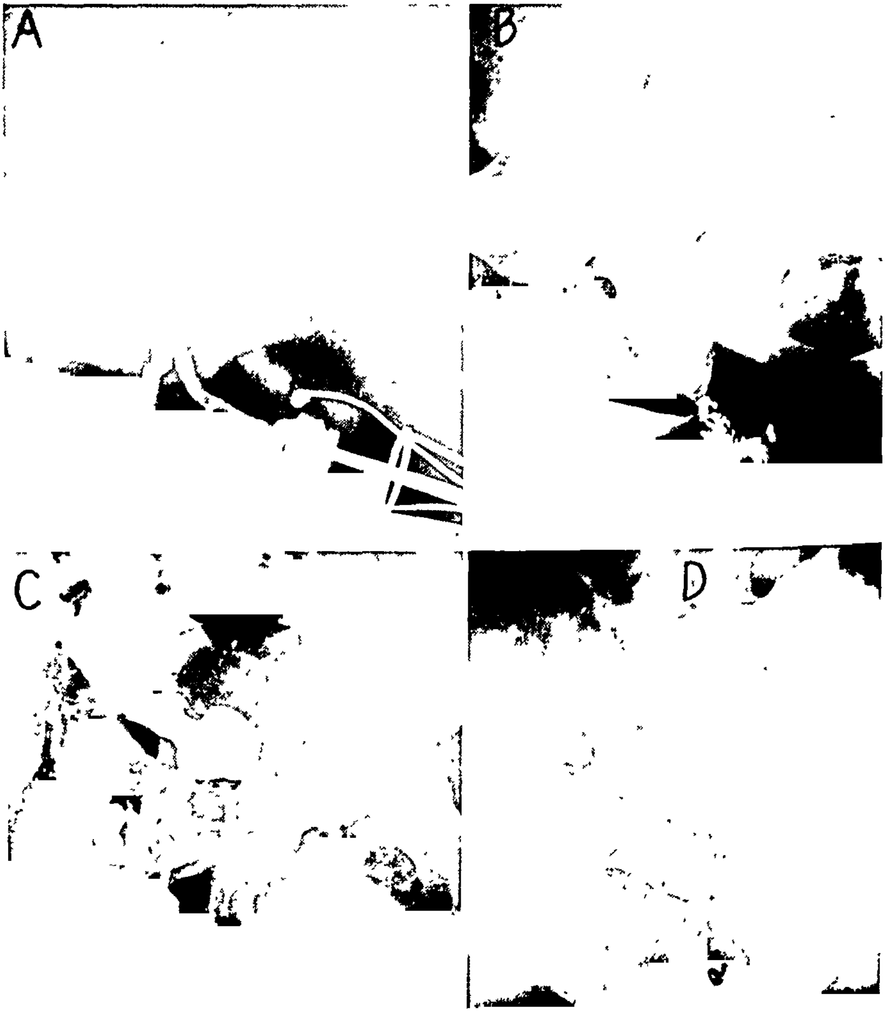

FIG. 5. *A*, urethral fistula. Urethrogram taken in presence of unhealed external urethrotomy. Marked narrowing in distal portion of urethra is seen near hypospadiac meatus. *B*, rupture of urethra. Urethrogram reveals extensive dispersion of urethrographic contrast medium as a result of rupture of bulbous urethra. *C*, peri-urethral phlegmon. Urethrogram shows a large amount of contrast medium distributed in tissues distal to urogenital diaphragm and limited by Colles' fascia as a result of septic urinary extravasation. *D*, urethroprostatic reflux in diverticular or cavitary prostatitis. Urethrogram shows an irregularity and narrowing of bulbous urethra and extensive reflux of contrast medium into prostatic tubules and acini which are dilated. Such a configuration invariably denotes chronic prostatitis.

delivery of medium to venous channels leading more directly to major veins and the inferior vena cava that would make available a route for rapid pulmonary oil embolism. If the fact is accepted that the erect penis is engorged with blood as a result of decreased venous drainage of the organ, then the oily contrast medium which invades the pooled venous channels resides more or less stationary until the flaccid state ensues. Gradual drainage of the penis and slow progression of the medium into the major venous channels follow. If local increased vascularity exists in urethral disease it is possible that the factor of vascularity influences the extent and distribution of intravasated urethrographic contrast medium.

THE FACTOR OF VISCOSITY OF OILY MEDIUM IN THE CIRCULATION

The viscosity of contrast medium would presumably play a part in the behavior of circulatory transportation. Its significant effect would concern the rate at which the medium travels through the venous system and the amount delivered to various destinations per unit of time. If a factor in the production of fatal pulmonary embolism due to air, oil or other liquid media is the amount of medium per unit of time delivered to the lungs, then the viscosity of oily medium which conceivably effects the rate of intravascular transportation by virtue of its adhesion to the venous walls and valves determines the amount of contrast medium per unit of time delivered to the pulmonary vascular bed. It is hardly likely that the frequently occurring potential opening of a patent foramen ovale would provide communication for a highly viscous oily substance. Under any circumstances the property of viscosity would presumably be that of retarding the progression of contrast medium and attenuate the production of fatal pulmonary oil embolism. It is also reasonable to appreciate that larger oil globules can obstruct larger pulmonary vessels. Air in the circulation probably encounters arteriolar or capillary arrest and depends upon the quantity delivered to the lungs per unit of time. A solid embolus such as blood clot probably produces a pulmonary effect in proportion to its size and the caliber of the pulmonary vessel occluded. The contour of oil globules may assume the shape of the vessels in which they are traveling, remain elliptical in shape or by conglomeration of numerous globules assume the shape, though not necessarily the size of a propagated blood clot. In all likelihood the size of oil globules and the quantity of oil delivered to the lungs are decisive factors and the product of these two factors is probably a constant for oily contrast medium in the production of fatal oil embolism.

THE FACTOR OF QUANTITY OF CONTRAST MEDIUM IN THE PRODUCTION OF EMBOLISM

In a personal communication Martland expressed the view that the introduction of 200–300 cc of air into the venous circulation was required for the development of fatal pulmonary air embolism. The total amount of oily contrast medium required for urethrographic study is 20–30 cc. The anterior male urethra has a capacity of approximately 20 cc. If in this and other series of urethrograms 20 cc of medium is observed in the anterior urethra there remains only approximately 5–10 cc of contrast medium available for entrance into the venous channels. It is difficult to appreciate that much more than 1 cc of oily urethrographic contrast medium gains entry into the circulation in cases of venous invasion during urethrography. It makes for perplexing comprehension to conclude that more than several cubic centimeters of intravasated oily contrast medium is necessary to produce death in the light of the record of fatalities from urethrography with the use of an oily medium. There presents the consideration that the quantity of medium which invades the circulation should apply to that quantity delivered to the lungs per unit of time and not to that quantity introduced into the circulation. Oil medium, in particular, entering a complex, interwining system of veins and sinuses may have a sluggish motility and an affinity to traverse numerous, divergent and complex patterns of venous channels. In the final analysis the occurrence of fatal pulmonary oil embolism presumes the occlusion with oil of a sufficient number of pulmonary arterioles and capillaries.

URETHROGRAPHIC CONFIGURATIONS OF THE IMPAIRED URETHRAL WALL

It is difficult to ascertain the degree and variety of impaired urethral structure and thereby assess the extent of extravasation of urethrographic contrast media. It is likely that the greater the defect and deficiency of the urethral wall the greater the possibility for the production of extravasation and intravasation. Many types of urethral disease reflect themselves urethrographically in some form of extravasation of contrast medium.

The most distinct type of breach of integrity of the urethra probably exists in the nature of urethral fistula. Urethral disease, in the form of an actual break in the continuity of the urethra, is the predominant factor in such extravasation. Minimal pressure is required for the invasion of urethrographic medium into the readily accessible urethral sinus tract (fig. 5, *A*). The not uncommon urethral fistulas which result from gonorrheal stricture provide conditions in which urethrographic medium is easily extravasated. Thus, urinary fistulas demonstrate a great degree of impairment in the continuity of the urethral wall and disclose that the degree of pressure, rate of injection and quantity of medium used assume minor roles in the production of invasion of urethrographic contrast media.

Other breaches of urethral continuity present themselves urethrographically in rupture of the urethra and in septic and nonseptic urinary extravasation (fig. 5, *B* and *C*).

The most common type of extravasation in urethrography is urethroglandular invasion. Chronic prostatitis affords the most frequent condition represented by glandular invasion of urethrographic contrast medium (fig. 5, *D*). This type of urethrographic distribution of contrast medium presumes an abnormal patency of prostatic duct orifices in the posterior urethra and dilatation of the drainage system of the prostate gland as a result of the effects of inflammation. The dilatations of the acini often appear as diverticula or cavities, and the designation of diverticular or cavitary prostatitis is a properly expressed urethrographic diagnosis. The question arises as to the effect of pressure and the possibility of artificial over-distention of the prostatic acinotubular system. Mechanically induced acinotubular distention as in the manual induction of "hydronephrosis" in retrograde pyelography probably can be produced, but is hardly likely inasmuch as an exceedingly pronounced type of vesical neck obstruction would be required to impede the flow of medium into the bladder and create sufficient intra-urethral pressure within the prostatic urethra to divert the medium into the prostatic ducts.

Tuberculous prostatitis provides an easily productive urethrographic pattern of diverticular or cavitary prostatitis (fig. 6, *A*). The familiar endoscopic picture of trabeculation in the posterior urethra with numerous interposed "golf-hole" prostatic duct orifices among the coarse fibromuscular intertwining strands reveals the accessibility of urethrographic medium to the prostate gland. It would seem that prostatic diverticula, though not pathognomonic of tuberculous prostatitis because of a similar urethrographic picture in nonspecific prostatitis, are nevertheless strongly suggestive of genital tuberculosis.

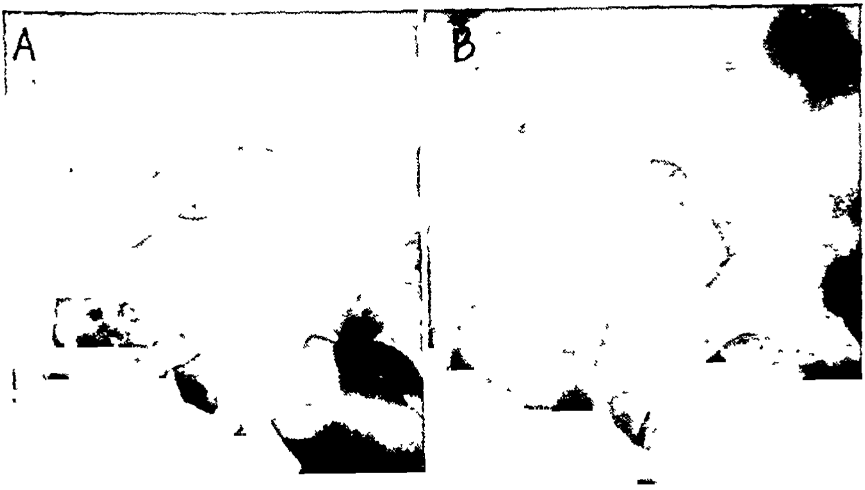

FIG. 6. *A*, urethroprostatic reflux in tuberculous prostatitis. Urethrogram shows saccular dilatations of prostatic ducts and acini, a small bladder and presence of contrast medium in right ureter, latter being unusual in urethrography. *B*, calculous prostatitis. Urethrogram shows presence of calculi and contrast medium incorporating most of prostatic adenoma.

Prostatic calculi, particularly those within the parenchyma, are prone to induce an irritative response on the part of prostatic tubules and acini and produce a degree of chronic prostatitis (fig. 6, *B*). Diseases of the prostate, such as nonspecific, tuberculous and calculous prostatitis herewith demonstrated urethrographically, reflect themselves by some degree of irregularity in structure of the posterior urethra and its contained ducts. It is not presumptuous to regard a normal posterior urethra and prostate gland impervious to the reflux of urethrographic contrast media.

The mucosal and submucosal glands partaking in those infectious processes which have predilection for the anterior urethra are frequently demonstrable on urethrograms. Not infrequently subsequent urethrograms taken after a period of urethral dilatation demonstrate a disappearance of glandular invasion of urethrographic medium to signify a regression of the infectious process and adequate drainage of the urethral glands.

Urethral diverticulum of the rare congenital variety or uncommon acquired type presents a distinct outpocketing from the lumen proper of the urethra. Urethral calculus is probably one of the most common causes of acquired urethral diverticulum (fig. 7).

THE RELATIONSHIP OF HEMATURIA AND INTRAVASATION IN URETHROGRAPHY

The presence of hematuria has frequently been proposed as a contraindication to the performance of urethrography. It seems unusual that the presence of hematuria should disqualify the use of this particular urological diagnostic procedure in the light of the liberal application of almost every type of manipulative diagnostic and therapeutic urological method in the presence of active and profuse bleeding. Venous invasion of variable amounts of a multitude of substances occur in the course of study and treatment of genito-urinary disease. Well known is the tremendous influx of substances into the blood stream in the presence of open venous sinuses during endoscopic surgery with the sometimes fatal complication of acute renal insufficiency. It is reasonable to assume that the presence of open venous channels affords a greater possibility of intravasation than intact venous channels, and the greater and more numerous the exposure of open veins the greater would be the degree of venous invasion. Venous invasion is noteworthy for its occurrence in the absence of urethral bleeding. The diseased urethra in the presence of bleeding or not is notorious in its generous absorption of obnoxious agents with the production of the so-called urethral chill or urethral fever. Intravasation is theoretically a greater possibility in the presence of urethral bleeding which denotes a defect in the continuity of the urethral wall. In general, venous invasion in urethrography would be expected to present an exceptional complication in the presence of hematuria provided excessive pressure is not used.

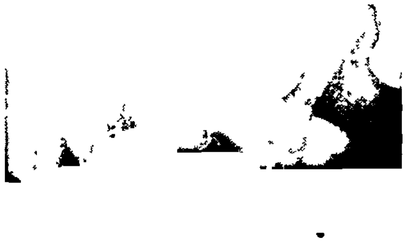

FIG. 7. Urethral calculi. A plain x-ray shows four circumscribed opacities in anterior urethra. One calculus produced a small urethral diverticulum.

COMMENT

Since a goodly number of disease entities of the lower urinary tract reflect themselves in an extra-urethral distribution of contrast media urethrographic study serves a useful supplementary or supportive diagnostic measure in the evaluation of urinary tract abnormalities. The limitations of urethrographic diagnosis are probably no greater than those of pyelo-ureterographic interpretation. The absence of demonstrable deformity in a urethrogram does not rule out the presence of disease of the urogenital tract. Foreign body reactions resulting from injection of urethrographic medium into the tissues or sequelae in the nature of paraffinoma of the penis resulting from the injection of paraffin into the tissues have not been observed.

The mechanism of venous invasion incorporates a combination of factors exclusive of the necessary element of impaired urethral structure. The effect of pressure during the performance of urethrography is probably the most significant factor invoking extravasation or intravasation as a result of urethral disease. The determination of the amount of pressure being utilized in the performance of urethrography finds no practical usefulness and renders no beneficial information with regard to the prevention of venous invasion of radio-contrast medium. Venous invasion can be induced by any degree of pressure. An estimation and appreciation of the degree of pressure is as readily ascertained in urethrography as in retrograde pyelography. A comprehension of the degree and extent of urethral disease would be the hypothetical index by which to predict invasion of medium. Since urethrography is used in the presence of urethral disease excessive pressure should be used at no time. There may often occur that variety of urethral disease which can tolerate excessive pressure, but there is never any accurate appraisal of the severity of urethral injury. An analogy may be made to the operative and postoperative irrigation of the bladder in endoscopic surgery. The integrity of the prostatovesical continuity of musculature cannot be thoroughly evaluated, and it is safe not to induce excessive intravesical pressure at operation or postoperatively in the presence of a poorly draining or occluded urethral catheter lest extravasation ensue as a result of a weakened and morbid vesical neck. The influx of a multitude of agents into open venous sinuses can probably be appreciably reduced by the avoidance of repeated excesses of intravesical pressure during endoscopic surgery. The effect of pressure is instrumental in the introduction of medium into the circulation where other factors related to the physical and chemical properties of blood and foreign medium supervene.

The significant circumstance in venous invasion is not the amount of oily contrast medium used in the urethrographic procedure or the amount of oil in the circulation but the quantity of oil delivered to vital foci of the body per unit of time. The fundamental disturbance is the effect of mechanical occlusion of blood vessels with oil at arteriolar or capillary gradations or the deleterious chemical effect of oil in capillaries and tissues. The relatively acute congestive disturbance and cellular infiltration and edema as seen in the pulmonary vascular bed and alveoli may represent a reaction to an obnoxious constituent of the oil in the form of an intolerable fatty acid. The nature of the oily medium used, therefore, could presumably determine the absence or presence and degree of harmful effects on the organism. It is possible that a large quantity of one type of oil in the blood stream may not produce as great a reaction as a smaller quantity of another type of oil. A recent report of a case of pulmonary embolism as a result of injection of penicillin in oil and wax included the remark that penicillin in peanut oil had not been known to produce a similar complication. Lipiodol, for example, is noteworthy in its participation of fatal pulmonary oil embolism while iodochloral which contains peanut oil has been demonstrated in the venous system but has not been known to partake in fatal embolism or nonfatal pulmonary embolism. The behavior in the blood of various oils such as peanut oil, cottonseed oil, mineral oil and the like is presumably different. Blood contains suspensions of fat globules of various dimensions under physiological conditions. The fatal oil or fat embolism as a result of fracture of bone or trauma to fatty tissue is probably due to the liberation of a certain type of fat constituent not handled well in the circulation. Serious cases of fat emboli will show considerable amount of fat in stained specimens of urine. Fat or oil emboli manifest clinical differences. Fat emboli characteristically cause no symptoms or death until after 24 to 48 hours but the fatal complications in oil embolism occur within several hours.

CONCLUSIONS

Urethral disease is a prerequisite for the production of extravasation or intravasation of urethrographic contrast medium. Disease of the bulbomembranous portion of the urethra is particularly receptive to the invasion of medium.

The use of excessive pressure will not induce invasion of contrast medium into the normal urethra.

Excessive pressure is not required for the production of venous invasion and should not be used in the presence of suspected or known urethral disease.

The characteristics of oily contrast medium, the idiosyncrasies of its behavior in the circulation and the quantity of oil delivered to vital foci of the body per unit of time determine the occurrence and severity of embolic phenomena.

Numerous urethral disease entities may be specified urethrographically as a result of the common occurrence of extra-urethral distribution of urethrographic radiopaque contrast medium.

Four cases of venous invasion are reported.

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REFERENCES

Axelrod, M.: Pulmonary embolism following injection of penicillin in oil and wax. J. A. M. A., **142**: 802–804, 1950.

Carr, J. R. and Johnson, C. M.: Fat embolism following instrumentation and injection of oil into the urinary bladder. J. A. M. A., **104**: 1973–1975, 1935.

Crabtree, E. G.: Venous invasion due to urethrograms made with lipoidal. J. Urol., **57**: 380–390, 1947.

Gaudin, H.: Fatal embolism following urethrography. J. Urol., **62**: 375, 1949.

Martland, H. S.: Air embolism. Am. J. Surg., **68**: 281–286, 1945.

Martland, H. S.: Personal communication. March 1950.

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THE INTERPRETATION OF TRANSLUMBAR ARTERIOGRAMS

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The visual study of the vascular pattern of living tissues and organs is not a recent development. As early as 1930, the vascular pattern of the kidney was studied by means of injecting a contrast medium into the abdominal aorta and recording the arterial pattern with the roentgen ray. Studies of this type have involved techniques that, at times, have appeared to be rather formidable. Many urologists have looked upon these techniques with fear and apprehension and, as a result, this field of investigation has not received the attention that its importance merits.

A desire to have a definite record of the anomalous vessels, which we have thought to be the cause of renal pain in certain patients without evidence of urinary tract obstruction, caused us to begin a study of the renal vascular pattern as determined by translumbar arteriography. This study began about two years ago and caused us to alter the previously described techniques. We are now using one which we have previously reported and which, in our hands, has produced neither fatality nor morbidity.

Although, during the past two decades, the procedure of translumbar arteriography has been discussed by several other investigators and several have described the characteristics of the arterial pattern found in certain types of renal disease, we have been unable to find a record of any attempt to describe and classify the normal patterns to be expected in various types of renal changes. For this reason, we recently selected for such a study, a group of approximately 200 arteriograms that were made upon patients in whom there was renal disease. From that study we believe that we can recognize certain definite changes in the arterial pattern which indicate specific types of renal abnormality.

The interpretation of a translumbar arteriogram requires a complete knowledge of the anatomy of the abdominal aorta and its branches as well as a detailed study of the arteriogram to be interpreted. It is essential that one trace each artery carefully from its origin to its termination in order to identify accurately each vessel's true anatomic position. One of the most difficult types of arteriograms that one is called upon to interpret is that in which there occurs a superimposition of a number of arteries, because at times, accurate identification of each of these individual arteries is extremely difficult. Upon numerous occasions we have seen the celiac axis arise, or at least appear to arise, below the level of the renal arteries, causing the hepatic or splenic arteries to course upwards and across the area of the renal shadow, as well as the arterial supply to the kidney. This can result in an improper interpretation of the arteriogram if a careful, intensive study is not carried out. Enlargement of the spleen or liver often causes superimposition of the splenic or hepatic artery upon the renal artery and the shadow of the renal parenchyma. The interpretation of the presence of

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an aberrant renal vessel must be made only after a very careful examination; the relative position of the supposed aberrant artery and the kidney shadow must be determined; the origin and termination of a suspected vessel must be thoroughly studied. The course of the suspected anomalous artery must be accurately followed to determine that it does not extend beyond the renal shadow and is traceable to its termination. We should be able to recognize the typical

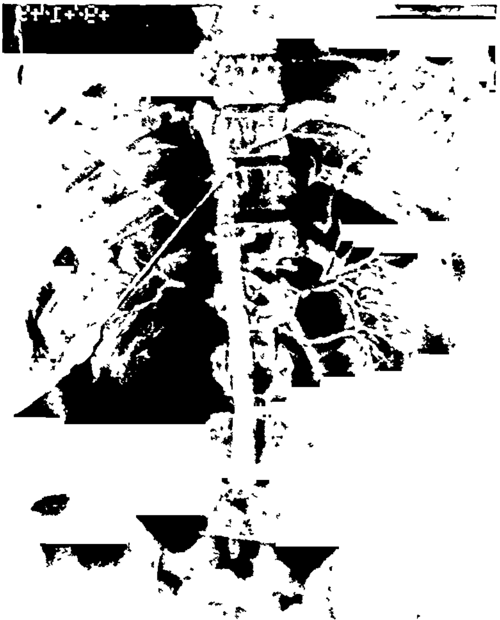

FIG. 1. Translumbar arteriogram illustrating type of arterial pattern obtained by injection of contrast medium directly into aorta. Note 1) celiac axis, 2) superior mesenteric, 3) renals and their distribution, and 4) an aberrant lower pole right renal artery.

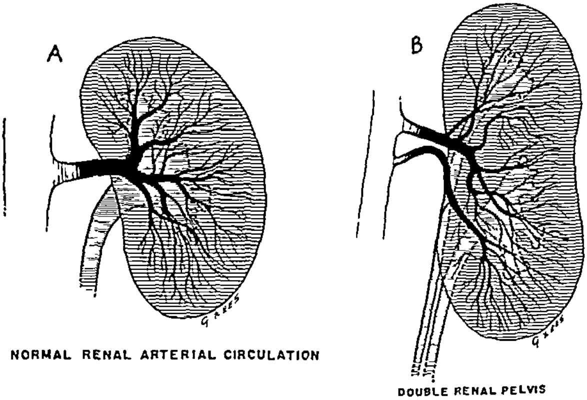

FIG. 2. *A*, schematic representation of normal renal arterial circulation. From studying a large series of normal renal arteriograms, this is pattern that we believe is normal. Note "fanning out" of terminal branches which are uniformly distributed throughout renal parenchyma. *B*, schematic representation of a normal pattern of a kidney with complete bifurcation of renal pelves and ureters

fan-like arrangement of the end arteries that is found only in the kidney. The lumbar arteries, shortly after departing from the aorta, turn posteriorly to enter the back muscles. Because of this rather acute angle just lateral to the vertebral body, they can be easily recognized.

THE NORMAL RENAL ARTERIOGRAM

The renal arteries branch from the aorta at the level of the L-2 vertebral body and are at right angles to the aorta. The primary division of the renal artery occurs just within, or close to, the hilum of the kidney. From this point the branches spread through the kidney with diminishing caliber. The small renal branches arise at acute angles and the interlobar and arcuate branches pass between the pyramids and spread out in graceful, minute curves in the cortex—a so-called fan-like arrangement. The normal arteriogram is illustrated in figures 1 and 2,A but it is, of course, to be understood that the incidence of more than one renal artery is extremely high.

THE ABNORMAL RENAL ARTERIOGRAM

We will first consider abnormalities of distribution due to congenital abnormalities of number or position of the kidneys and their pelves and ureters. Arteriography in this type of case gives a vast amount of information that is of great value to the clinician as it is the only method by which one is able to learn the number and location of renal arteries, a matter of extreme importance in those cases of congenital anomalies that require surgical care.

Bifurcation. Bifurcation of the renal pelvis usually has associated with it a multiplicity of the renal arteries. The importance of a preoperative knowledge of the number and location of these accessory renal arteries is, of course, apparent to anyone (fig. 2,*B*).

Congenital ectopic kidney. The congenital ectopic kidney, pathologic or otherwise, frequently requires the carrying out of surgical procedures. Experience and, more concretely, arteriograms of such cases have demonstrated the high percentage of these patients who have associated anomalous vessels. Frequently, the arterial supply arises not only from the normal position in the aorta, but also from the common iliac artery and occasionally, even from pelvic vessels on the opposite side.

Crossed renal ectopia. Here again, arteriography is of great benefit if we are contemplating surgery, for in two patients recently examined, in one we found four renal arteries arising from the lower abdominal aorta and one from the common iliac of the side opposite to the location of the kidney. The other patient, whose pyelogram was almost exactly the same, had only one renal artery. That vessel arose from the normal position of the renal artery on that side, entered the upper pole of this kidney mass and supplied the lower as well as the upper portion. Certainly, information such as this is of great value (fig. 3,A).

Horseshoe kidney. Arteriography is probably of greater value in planning surgical procedures of a horseshoe kidney than in any of the congenital anomalies, for this anomaly is characterized by a great variation in the distribution of the renal arteries. By personal communication, we have learned of one case with horseshoe kidney in which at autopsy, only one renal artery was found (fig. 3,*B*).

Hypoplastic kidney. We, as everyone else, have been extremely interested in the hypoplastic kidney and its importance in vascular hypertension. It is frequently impossible to catheterize the ureter of these hypoplastic kidneys and, as they are not visualized by excretory urography, the procedure of translumbar arteriography assumes an important role because it is the only method that will determine whether there is a remnant of kidney present in the renal fossa or not. Five cases of hypoplasia have been studied by arteriography. In three, the only method that allowed us to determine that there was a hypoplastic kidney present was the arteriogram (fig. 4,*A*).

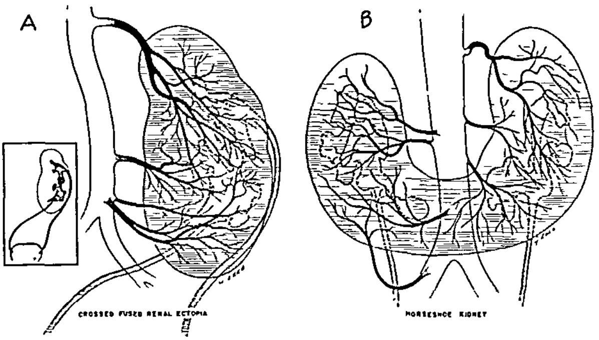

FIG. 3. *A*, schematic representation of a complete, crossed, fused renal ectopia. This is what might be called normal pattern of arterial supply, but there is great variability of arterial pattern in this interesting anomaly. *B*, a great number of arteries usually enter horseshoe kidney and great variability exists in their point of origin.

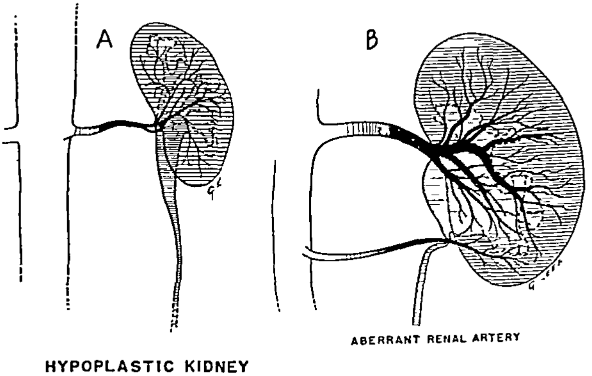

FIG. 4. *A*, as one would expect, this schematic representation shows very small artery with very few branches and a lack of typical "fanning out." *B*, schematic representation of manner in which an aberrant artery (especially if it arises directly from aorta) could produce torsion of kidney and compression of renal vein.

Renal hypertension. It is generally agreed that there is a substance produced in the renal parenchyma under certain circumstances that when absorbed into the general circulation acts as a pressor substance producing otherwise unexplainable arterial hypertension. Hypertension has resulted from the production of such a substance following the partial compression of the renal vein as well as by the better-known ischemia following similar partial compression of the renal artery. The presence of an anomalous vessel in a patient whose kidney has an abnormal amount of mobility may result in a torsion or twisting of the pedicle in such a way as to compress, in a similar manner, the thin-walled vein upon the rather rigid artery and thus produce a pressor substance responsible for the production of hypertension. We believe that we have recognized three such cases; at least in our series there were 3 patients who had marked hypertension, in whom anomalous vessels were ligated and the renal position corrected, who have recovered from the hypertension. Although we certainly wish to draw no conclusions from such a very brief series of cases, it is one that warrants our interest and continued study (fig. 4,*B*).

Renal infarction. Our experience with arteriography in renal infarction has been extremely illuminating. We have been unable to find any reference to renal arteriographic studies in this type of case. As a result of the study of five patients with proven renal infarction, we believe we have been able to establish a pattern which will allow the diagnosis of this condition. Four of these five patients had malignant hypertension, one of 280/160. (To illustrate our feeling of security about the safety of this procedure, we had no hesitancy in doing a translumbar arteriogram after the anesthetist said he would assume responsibility for the anesthetic.) In four of these patients, three of whom had multiple large infarcts and one a single massive infarct, we saw exactly what one would expect, a sharp termination of the artery or arteries and a comparatively avascular area between that point and the periphery of the kidney, there being no associated curving or circling of the small arteries, as is sometimes seen in cystic disease. In one of these patients, who at autopsy was found to have innumerable small renal infarcts, the arteriogram was not characteristic, although on close study it was noted that we could not trace the arteries out as far as in the usual case (fig. 5,*A*).

Hydronephrosis. In hydronephrosis, the caliber of the main renal artery is important in evaluating the renal arterial supply but by studying the terminal branches of the renal artery, greater information is available. As seen by us, the renal arteries have phases of filling on serial films made with a rapid casette changer. However, it was usually possible, by the single film technique, to distinguish between actual decreased circulation and incomplete filling by studying the terminal branches of the renal artery. If they were clearly seen and moderately opaque, yet spread apart and few in number, the circulation was considered impaired.

If the renal parenchyma is replaced by chronic infection and/or hydronephrosis, the arterial supply to the renal parenchyma is decreased. Believing that the amount of circulation to the kidney is an indication of the potential renal function and the ability of the kidney to recover, we have utilized translumbar arteriography as a measuring stick for therapy and prognosis in patients with hydronephrosis. In addition, it is informative in ureteropelvic obstruction to determine the presence or absence of an aberrant artery. In all patients requiring surgery because of hydronephrosis, we utilize arteriography. Our experience, although limited to amount and length of follow-up, has borne out our belief that arteriography is a valuable method of evaluating potential renal function (figs. 5,*B* and 6,*A*).

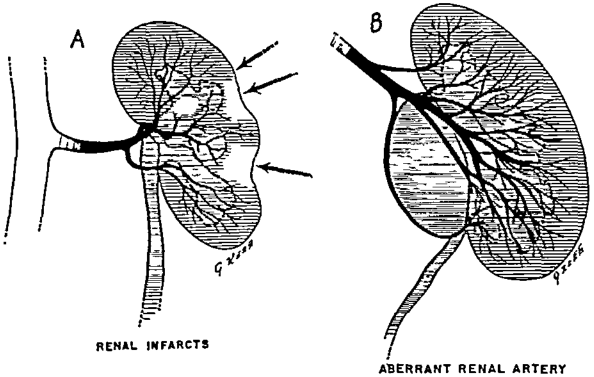

Fig. 5. *A*, It is to be noted that there is a very characteristic sudden termination of arteries in region of infarcts with an area of avascularity between their termination and renal capsule. *B*, schematic representation of manner in which an anomalous branch of renal artery can produce obstruction at ureteropelvic junction with resulting hydronephrosis. Note that arterial pattern is otherwise normal and, in spite of amount of hydronephrosis, arterial pattern indicates that there is sufficient renal parenchyma to warrant conservative surgery.

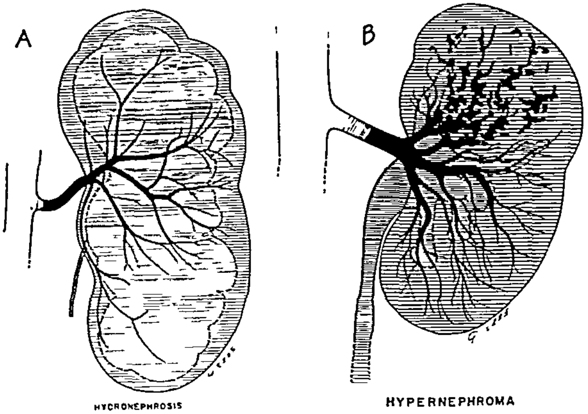

Fig. 6. *A*, advanced hydronephrosis which in this case results from ureteropelvic stricture and presents this typical pattern characterized by an absence of normal "fanning out" of terminal branches. *B*, schematic representation of characteristic "pooling" or "puddling" of contrast medium in region corresponding to filling defect on retrograde pyelogram, that is found in vascular parenchymal tumors

Ureteral obstruction. The procedure of arteriography has been of value in 8 patients with completely obstructed ureters. In these patients, four had normal renal arterial supply and four had diminished arterial supply. All of the latter 4 patients had nephrectomies and the renal parenchyma in each instance was severely damaged or replaced. In the 4 patients with normal arterial supply, the ureteral obstruction was relieved and there has been a return to normal renal function by each kidney.

Probably one of the most practical values of translumbar arteriography is its great worth in the differential diagnosis between tumors and cystic disease of the renal parenchyma. In this series there were 26 cases in which arteriography was used in the differential diagnosis and, although we were not keen enough to properly interpret all of our arteriograms prior to surgery, a latter review of those in which a mistake was made showed that the arteriogram had not failed but that we had. In other words, the arteriogram in each of those cases supplied the information that, when properly interpreted, provided a correct preoperative diagnosis. The key upon which proper interpretation is based is the simple fact that parenchymal tumors are vascular structures, and that cysts, solitary or polycystic, are not.

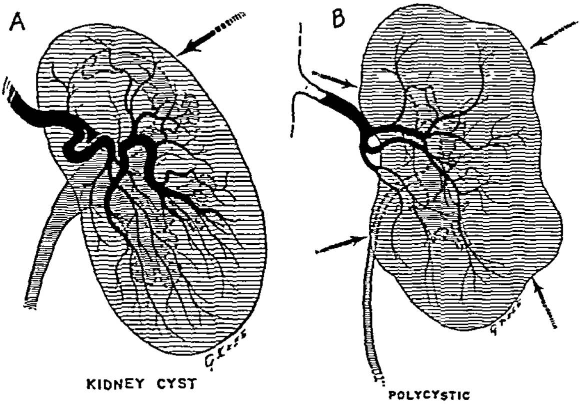

FIG. 7. *A*, in spite of very marked deformity of renal pelvis, characteristic area of avascularity and lack of "puddling" in region of filling defect confirms diagnosis of cystic disease. *B*, schematic representation of wide dispersion of small arteries and failure to visualize terminal branches is characteristic of this disease and is confirmatory evidence of diagnosis.

Renal tumors. As the tumor is vascular and contrast medium will, of course, follow the arterial stream, there will be a "pooling," "laking" or "puddling" of the contrast medium in the area of the lesion indicated by pyelography. One may even note some irregularity of the vessels within the tumor, but this is not a constant finding. On one occasion, this "pooling" or "puddling" of the contrast medium led us to make a diagnosis of a small tumor in a patient with recurrent hematuria in whom we were unable to demonstrate any change in the pyelogram. On exposure of the kidney, a tumor less than 2 cm. in diameter was found immediately beneath the capsule in the area indicated on the arteriogram (fig. 6,*B*).

Tumors arising from the epithelium of the renal pelvis and invading the renal parenchyma may show a slight change in the vascular pattern, but seldom demonstrate any tendency to "pooling" or "laking." We have been unable to recognize any characteristic pattern that would aid us in the diagnosis of this type of tumor. Other workers have previously come to the same conclusion.

Solitary renal cyst. In patients with solitary renal cysts a comparatively avascular area in the region of the filling defect, as shown on the pyelogram, was present in every case. We have frequently observed rather small arteries overlying a portion of this area. These represent small vessels immediately adjacent to the parenchymal portion of the cyst. In no case was there any suggestion of "pooling" or "puddling" of the contrast medium in the region of the filling defect shown in the pyelogram. In addition, in several of these patients there seemed to be a definite curving of the vessels around the avascular area. One observation, that we have no record of having noted before, is that the nephrogram which is taken immediately following the arteriogram, very frequently shows an area of "thinness" of the renal shadow in the region of the cyst which, of course, is what one would expect to find (fig. 7,*A*).

Polycystic kidney. The arterial pattern that is seen in polycystic kidney demonstrates a spreading out of the entire pattern and a tendency toward the disappearance of the terminal branches producing areas of very definable avascularity (fig. 7,*B*).

DISCUSSION

Arteriography is of great benefit in determining the renal pattern in all types of congenital anomalies. Preoperative knowledge of this arterial pattern permits a more accurate surgical plan and a less tedious surgical procedure in that the location of these vessels is known prior to surgery. In those cases where partial nephrectomy or ligation of anomalous vessels is contemplated, arteriography is of especial value.

We believe that a further study of the renal pattern in renal hypertension of various types has promise of providing information of great value.

Translumbar arteriography is a method by which one can definitely determine the salvagability of the renal parenchyma for the axiom that "the kidney is no better, but just as good as its blood supply" is one to be remembered.

In our series, arteriograms have never failed to give the differential diagnosis between cystic disease of the kidney and parenchymal tumors. Certainly, the accuracy of that differential diagnosis has not been very high with the commonly used procedures.

In conclusion, we wish to emphasize that the procedure of translumbar arteriography is one that can be used with a feeling of security and that, as experience in interpretation of these films is accumulated, we will be in a good position to appreciate more fully the value of this procedure.

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ERRATUM

May 1951 issue, p. 846: Line 10, change 100 r to 1200 r_y.

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PHEOCHROMOCYTOMA: REPORT OF A MALIGNANT CASE (PHEOCHROMOBLASTOMA)

FRANK J. PYLE

We shall consider only the medulla of the adrenal glands. The medulla is vascular, soft, pulpy, and is dark brown or red in color. It is rich in nonmedullated post-ganglionic nerve fibers, and there are a few sympathetic ganglion cells within its substance. The nerves are mainly derived from the splanchnic sympathetic and a few from the phrenic and vagus. It is composed in most part of finely granular chromaffin cells from which adrenalin is extracted. The arterial supply comes from the aorta, and the inferior phrenic and renal arteries.

Embryologically, the medulla is derived from ectodermal cells developing from the primordial ganglionated cord of the sympathetic nervous system. At first it is outside the cortex but gradually becomes embedded within its substance, until completely surrounded by cortical tissue. During the fourth month, the cells take on their chromaffin-staining characteristic.

In the adult the boundary between the cortex and the medulla is irregular. The cells themselves are irregular in shape and arranged in rounded groups, or in short cords, surrounded by sinusoidal venules. These cells undergo the "chromaffin" staining reaction characteristic of chromaffin tissues, all of which, in this case, manufacture adrenalin. Chromaffin tissue is not confined alone to the medulla, but is distributed throughout the ganglia of the sympathetic nervous system and the carotid and coccygeal bodies.

The hormone of the adrenal is epinephrin or adrenalin, first synthesized by Aldrich and Takamini. The secretion of adrenalin is actuated by the splanchnic nerves, which form a part of the sympathetic system and, conversely, the vagus and parasympathetic nerves inhibit its secretion. Adrenalin is the great sympathetic stimulant and it affects all organs and functions governed by the sympathetic system, the vegetative part of ourselves. Adrenalin secretion is stimulated by muscular activity, such hormones as thyroxin, and, to some degree, by insulin. This effect is heightened by emotional stress, extensive burns, and certain drugs. Among them, nicotine, morphine, ether, and chloroform, if repeatedly used or long continued, produce paralysis of the sympathetic and exhaustion of the adrenal medulla. The result is low blood pressure, low blood sugar, muscular weakness, and slowing of heart rate. Surgical shock also, notably ensues upon such depletion. Finally, the medullary tumor we are considering, pheochromocytoma, secretes adrenalin in large amount and produces the characteristic symptoms of hyperadrenalism.

The following changes result:

Stimulation of adrenal medulla or adrenalism (sympathetic stimulation)

1. Blood vessel constriction
    a. Hypertension
2. Heart stimulation
    a. Decreased rate (vagus stimulation)
    b. Increased force

Read at annual meeting, Southeastern Section, American Urological Association, Gulfport, Miss., February 3, 1950.

3. Uterine contractions
4. Intestinal function
   a. Decreased peristalsis
   b. Decreased digestive juice secretion
   c. Valve and sphincter contraction
5. Eye
   a. Pupil dilation
   b. Retraction upper lid
   c. Protrusion eyeball
6. Kidney function
   a. Increased function
   b. Polyuria
   c. Sodium, potassium, and phosphate excretion (variable)
7. Metabolism increase
   a. Hyperglycemia
   b. Increased heat production
   c. Increased oxygen consumption
8. Blood picture
   a. Decreased coagulation time
   b. Lymphocytosis
   c. Anemia
      1. Temporary increase in erythrocytes (splenic contraction)
      2. Later destruction R.B.C.
9. Muscle stimulation
10. Skin
    a. Arrectores piliexcitation
    b. Sweat glands—not stimulated
       1. Sweating from inc. bld. temp.
11. Bronchi
    a. Relaxed musculation (pulmonary edema)[1, 2]
    b. Increased respiration

Tumors of the adrenal medulla and of the chromaffin system in general are so rare that only a few are diagnosed before death. They arise from one of three types of cells in the medulla. The principal type of cell is the neuroblast or sympathagonia, and it is from sympathagonias that neuroblastomas develop. Sympathagonia divide into the neurocyte or nerve ganglion cell and the chromaffin or secreting cell:

Tumors of adrenal medulla

Sympathogonia
Neuroblastoma
- Neurocytes (nerve ganglion cells)
  1. Ganglioneuroma
- Chromaffin (secretin cells)
  1. Pheochromocytoma
  2. Pheochromoblastoma

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[1] Wolf, W.: Endocrinology in Modern Practice. Philadelphia: W. B. Saunders Co., 1939, 2nd ed.

[2] Best, C. H. and Taylor, N. B.: The Physiological Basis of Medical Practice. Baltimore: Williams and Wilkins Co., 1950, 5th ed.

Ganglioneuromas, consisting of nerve ganglion cells and found both in children and adults, are benign. Pheochromocytomas, consisting of chromaffin cells, in the adrenal medulla[3] or elsewhere in the chromaffin system, are rare. They are usually benign, but a few are malignant. These latter are the pheochromoblastoma.[4]

Pheochromoblastomas in the adrenal medulla secrete adrenalin, and the symptoms are those of hyperadrenalism. The chief symptom is paroxysmal hypertension. The symptoms are spontaneous or induced. They are: pounding headache, epigastric distress, palpitation, and cold hands, feet, and skin, all from the contraction of the peripheral arterioles. These symptoms may be brought on by fever, by emotions such as anger and fear, by injury, cold pressor tests, chemical agents, or, most noteworthy, by any change of posture that serves to massage the tumor. An attack is almost always followed by sweating, prostration, exhaustion, and sometimes outright shock. Associated are high blood pressure and, as a rule, hyperglycemia and glycosuria.

Experimentally, the same group of symptoms is induced by injection of histamine phosphate.[5, 6, 7] Roth and Kvale[5] applied this test following their observation of hypertension while a patient was receiving a histamine solution intravenously.[8] The dose ordinarily necessary is 0.05 mg. but on one occasion pheochromocytoma was suggested by the reaction following injection of 0.5 gm. during a gastro-analysis.[9] Under similar circumstance 25 mg. of mecholyl bromide will raise the blood pressure for 10 to 20 minutes.[6, 10] A hypertensive reaction lasting for 20 minutes can also be produced by injection of tetra-ethyl-ammonium chloride.[10] However none of these drugs gives any response following operation.

Adrenolytic drugs, especially benzodioxane (dimethyl piper-idionaminomethyl benzodioxane) are valuable in diagnostic testing for chromaffin cell tumor of the adrenal medulla.[6, 11, 12, 13] 20 mg. intravenously during an episode will lower the blood pressure for about 10 minutes. Dibenamine hydrochloride (dibenzl-beta-chlorethylamine) 7.0 mg. per kilogram of body weight lowered the blood pressure to normal for 24 hours.[11, 14, 15]

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[3] Cahill, G. F.: Hormonal tumors. Surgery, **16:** 233–265, 1944.

[4] Belt, A. E. and Powell, T. O.: Chemical manifestations of chromaffin cell tumors arising from suprarenal medulla. Surg., Gynec. & Obst., **59:** 9–24, 1934.

[5] Roth, G. M. and Kvale, W. F.: Tentative test for diagnosis of pheochromocytomas. Am. J. Med. Sc., **210:** 653–660, 1945; J. Lab. & Clin. Med., **30:** 366–368, 1945.

[6] Ganem, E. J. and Cahill, G. F.: Pheochromocytomas co-existing in adrenal gland and retroperitoneal space with sustained hypertension. New Eng. J. Med., **238:** 692–696, 1948.

[7] Saffer, L., Mencher, W. H. and Colp, R.: Symposium on surgical diagnosis of pheochromocytomata of adrenal gland; report of 2 cases with operative removal of tumor. Surg. Clin. North Amer., **26:** 368–381, 1946.

[8] Kvale, W. F., Roth, G. M., Clagett, O. T. and Dockerty, M. B.: Headache and paroxysmal hypertension.: Observations before and after surgical removal of a pheochromocytoma. Surg. Clinics North Amer., **24:** 922–933, 1944.

[9] Burrage, W. C. and Halsted, J. A.: Adrenal medullary tumor (pheochromocytoma). Case report with successful operation. Ann. Int. Med., **28:** 838–849, 1948.

[10] Bartels, E. C. and Kingsley, J. W., Jr.: Diagnostic approach to pheochromocytomata. Lahey Clinic Bull., **6:** 7–13 1948.

[11] Goldenberg, M., Snyder, C. H. and Aranow, H., Jr.: New test for hypertension due to circulating epinephrine. J.A.M.A., **135:** 971–976, 1947.

[12] Colston, J. A. C.: Bilateral familial pheochromocytoma. J. Urol., **59:** 1036–1058, 1948.

[13] Cahill, G. F. and Aranow, H.: Pheochromocytoma· Diagnosis and treatment. Ann. Int. Med., **31:** 389–404, 1949.

Diagnosis of pheochromocytoma depends on:

1. The symptom-complex.
2. An attack following immediately upon administration of an epinephrine secretion stimulating drug such as histamine.
3. Response to an adrenolytic or epinephrine antagonist such as benzodioxane.
4. Roentgenographic evidence of tumor as revealed by shadows indicating renal displacement, or by use of perirenal insuffiation, or by laminography.

CASE REPORT

Mrs. H. D., aged 57 years, was admitted to the Orange Memorial Hospital on February 23, 1949. She gave a history of peculiar spells over the past 5 years. (She stated she has been having mild attacks for 28 years.) These came on as often as twice weekly in the morning after arising and were characterized by epigastric pain, forceful heart action, and severe headaches. These are now accompanied by nausea and vomiting of saliva or clear fluid, flushing, and profuse sweating. Sneezing would abort the attack, or eating would often prevent a second attack. About 2 years ago she found that turning on her left side would start an attack similar to the above. About 2 weeks ago she had a severe attack of pain in her right flank while lifting a chair. This was accompanied by extreme hypertension (systolic up to 300).

The past history was of no import except that there was an examination in a clinic in 1946 and in 1947. Although the significance was not realized at the time, one of these attacks was brought on when she received an injection of histamine during a gastric analysis in 1946. There is no record of her blood pressure during that episode but her blood sugar was only 121 mg.

Physical examination on admission was essentially normal. She appeared underweight but not acutely ill. The blood pressure was 150/80 except when she turned on her left side. This began an attack with the blood pressure suddenly jumping to 220/130. A mass was palpable in the right hypochondrium and extended through to the costovertebral angle.

Urinalysis was normal except for an occasional finding of albumin. The blood count was normal except for secondary anemia. The blood sugar was 121 mg. per cent; the blood urea nitrogen was 10.6; blood chlorides 420; albumin 5.3; and globulin 1.9.

Cystoscopic examination was negative. However, the retrograde pyelograms revealed the right kidney to be rotated and displaced downward by a tumor mass (fig. 1, *A*). No evidence of metastases to the lungs was reported on chest x-ray but a review of these films suggests the possibility of early metastases at that time (fig. 1, *B*).

The benzodioxane test for pheochromocytoma was made by Dr. Fred Mathers of the Orange Memorial Hospital with the findings as recorded on the accompanying chart (fig. 2). The patient was turned on her left side which produced

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[14] Hecht, H. H. and Anderson, R. B.: Influence of dibenamine on certain functions of sympathetic nervous system in man. Am. J. Med., **3**: 3–17, 1947.

[15] Spear, H. C. and Griswold, D.: Use of dibenamine in pheochromocytoma (report of a case). New Eng. J. Med., **239**: 736–739, 1948.

a typical attack and a rise in the blood pressure to systolic 260 and a diastolic of 130. At this time 14 mg. of benzodioxane was injected intravenously. The blood pressure dropped at once to 150/90 and remained here for 15 minutes while the patient remained on her left side.

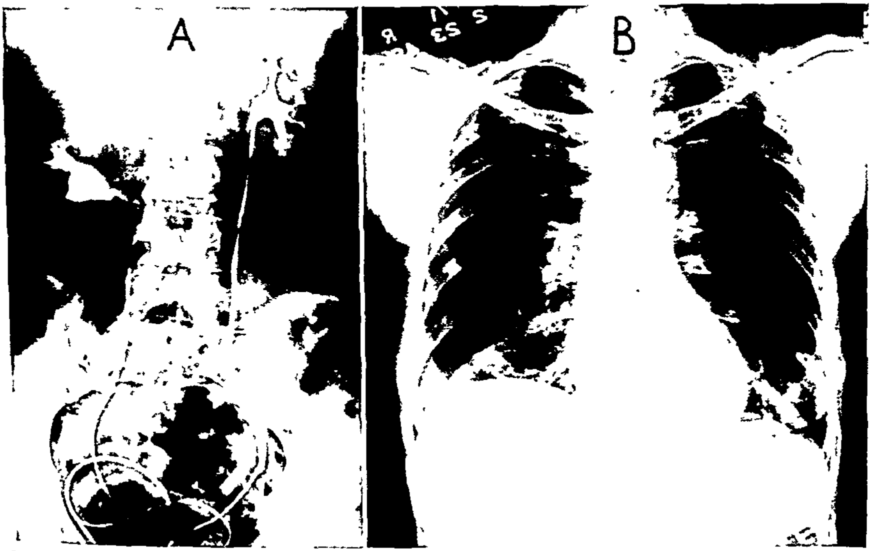

FIG. 1. *A*, Bilateral retrograde pyelogram showing displacement of right kidney by pressure from tumor. *B*, chest x-ray showing early (questionable) metastases about right hilus.

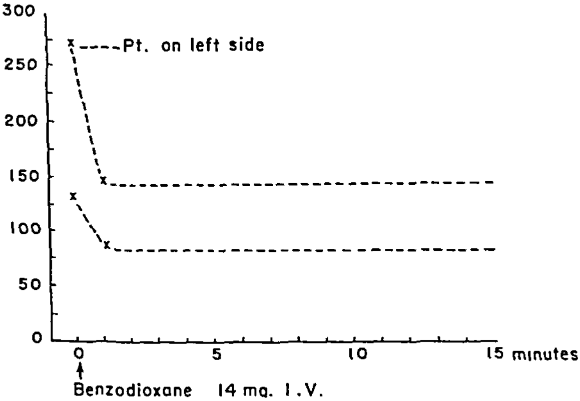

FIG. 2. Benzodioxane test for pheochromocytoma

An interesting observation in the electrocardiograms in this case was made by Dr. Mathers. He found that an electrocardiogram made with the patient at her basic level of blood pressure showed an inversion of T waves and a tracing taken during a seizure (with patient on her left side) showed an increase of the P-R interval from 0.14 to 0.20 seconds, a peaked and slightly slurred P2 and upright and normal appearing T waves. Following the operation the tracing revealed a return to normal. The case reported by Spear and Griswold[15] revealed a left axis deviation and inverted T waves in 1, 2 and 4.

An operation was advised and was performed on March 9, 1949. The choice of an anesthetic and operative approach presented difficulties. Dr. A. F. Shirmer, an Orange Memorial Hospital medical anesthetist, gave the patient pentothal sodium solution intravenously and supplemented this with nitrous oxide-oxygen. The patient was placed in a flat position lying on her abdomen since this position did not initiate an attack. The right side was elevated by the use of a sand bag and then an incision was made over the eleventh rib running from its attachment to above the crest of the ilium, the twelfth rib being only a very rudimentary one. This disection was continued through the subcutaneous tissue, clamping all bleeding points as encountered and ligating them. Following this, the external oblique muscle was cut through as was the internal oblique. The lumbar fascia was opened and the peritoneum reflected medially, splitting the transversalis fascia and muscles along their fibers. Following this, the ligament running from the vertebra to the eleventh rib was cut allowing this to be retracted upwards. The dissection was then continued in a posterior direction and down over the deep muscles of the back in order to avoid entering the peritoneum. Following this the tumor was identified and Gerota's fascia was opened. The kidney was found to be free and not involved in the tumor and could be separated from this large tumor mass with ease. At this point the patient's condition became rather serious as she had stopped breathing and her blood pressure had dropped to a very low point, as shown in this anesthesia record (fig. 3). This apparently followed clamping of the vessels that supplied the tumor mass. No definite pedicle could be identified, but at several points, large dilated veins were located entering the tumor mass. After the anesthetist had the patient under control, respiration resumed, and condition satisfactory, the operation was continued. The eleventh rib was removed in order to give sufficient space for removal of this large tumor. Following this, the tumor could be freed from its fossa and the remaining vessels entering the mass could be clamped as it was delivered. No excess bleeding was encountered although a large amount of general oozing occurred throughout. The tumor mass was removed complete and the fossa packed after the clamped vessels

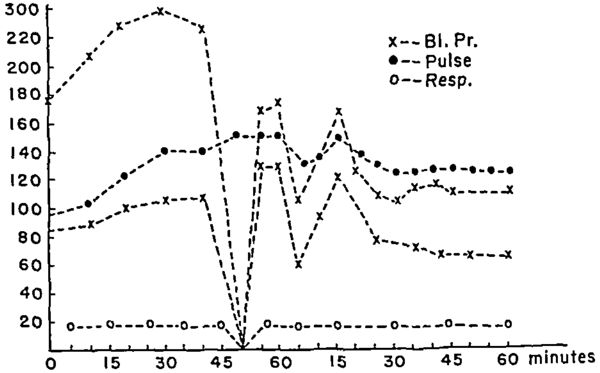

FIG. 3. Anesthesia record

entering at the assumed pedicle were ligated. Following this, two openings in the pleura were located where the eleventh rib had been removed. They were closed as thoroughly as possible and several other small bleeding points were clamped and ligated in the fossa. Packing was then placed in the fossa, and one cigarette drain introduced. Following this the kidney could be returned to its normal position with ease and it was allowed to remain in this position as it had not been interfered with at any time during the operation. Closure was then made in the usual manner. She was in fairly good condition at the end of operation and was returned to her room where she was placed in an oxygen tent and given 1500 cc of blood and at intervals over the next 6 hours, 2 units of plasma. Prognosis was fairly good following operation.

The pathological report, as made by Dr. George Kerr, pathologist at Orange Memorial Hospital was as follows:

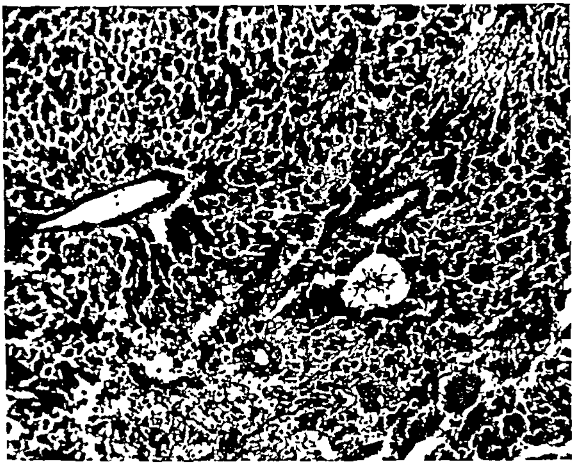

FIG. 4. Microscopic section from pheochromocytoma

"The gross specimen consisted of a large encapsulated tumor growth measuring 17.5 by 13 by 10 cm. The weight was 1070 gm. The capsule was partly torn in the region of its vascular attachment. A small amount of fatty tissue was present in that area. The surface of the growth was smooth and slightly lobular. Cut section showed soft, greyish tumor tissue throughout with many areas of hemorrhage. No definite brownish colored tissue was found. There was a central cystic space approximately 4 cm. in diameter which was filled with hemorrhagic fluid and fibrin.

"Microscopic study of the sections showed a cellular tumor composed of alveolar masses of malignant cells supported by fibrous vascular stroma. The cells were pleomorphic, many with indistinct cell outlines. Some cells appeared distinctly bipolar. Occasional multinucleated tumor giant cells were present. The cytoplasm was finely granular. The nuclei were hyperchromatic and there were numerous mitotic figures. In many areas the cells were arranged around central vascular spaces. Many areas of hemorrhage and necrosis were present. See figure 4.

"A section fixed in Zenker's fluid (containing potassium bichromate) showed chromation of an occasional cell. This was not so marked as one would expect, probably due to the acid present in Zenker's fixative or to the immaturity of the tumor cells.

"Sections of the extracapsular fatty tissue from the region of the attachment of the tumor showed no evidence of tumor spread. Diagnosis: Adrenal pheochromoblastoma."

The postoperative course was uneventful except for temporary weakness of the left arm which was no doubt due to the position in which it was needful to keep the patient during operation. Her blood pressure remained within normal limits. She had a mild hydropneumothorax on the right side but it disappeared before discharge on March 29, 1949. The incision had healed and the blood pressure was 120/80.

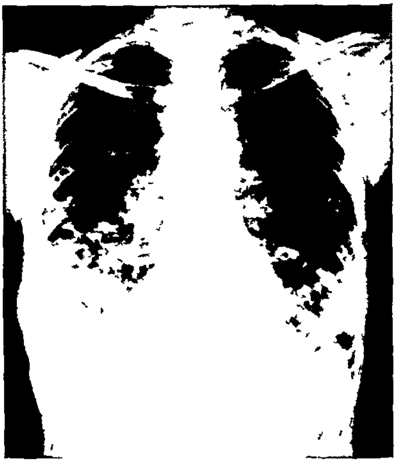

FIG. 5 Chest x-ray showing extensive lung metastases

Follow up examinations were normal until in August 1949, when the patient apparently had influenza while on a fishing trip. She became exhausted and developed marked dyspnea. She was admitted to the hospital on September 3, and physical examination revealed a large abdominal mass. X-ray (fig. 5) showed widespread pulmonary and bony metastases. She died on September 12, 1949.

The autopsy report follows: "The only external findings of note were 1) the presence of some abdominal distention, 2) the presence of a healed surgical scar in the right kidney region, and 3) the presence of coarse hair over the upper lip and chin.

"Both pleural spaces were studded with soft greyish tumor growth, many streaked with hemorrhage. The lungs were loosely bound to the parietal pleura on each side. The mediastinal nodes were found enlarged by soft similar tumor growth. The pericardial sac was essentially normal except for the presence of a few loose adhesions over the anterior surface of the right and left ventricle. No tumor growth was found in the pericardium.

"There was marked distention of the stomach and large intestine by gas. The liver was enlarged and contained numerous metastatic tumor nodules which projected from the surface. A mass of enlarged metastatic nodes was found in the region of the pancreas and portal area. A mass was also felt in the right adrenal region where there was also considerable scar tissue. There was no free peritoneal fluid and no metastatic implants were found over the peritoneum.

"The heart was normal in size. The cardiac valves appeared normal. There was no evidence of metastatic tumor.

"Both lungs contained large numbers of metatastic tumor growths, varying in size from a few millimeters to 2 cm. The tumors were soft in consistency and greyish-white in color. Many were streaked with hemorrhage. The lower lobes contained somewhat more tumor growth than the upper portions of the lungs.

"The spleen was normal in size and shape and free of tumor growth.

"The liver was somewhat enlarged and contained large numbers of metastatic tumor deposits similar to those seen in the lungs.

"The gallbladder appeared essentially normal.

"The pancreas appeared essentially normal although numerous large metastatic lymph nodes were present around the head of the pancreas.

"The stomach was greatly distended with gas. The small bowel appeared essentially normal. The large bowel contained considerable gas. No tumor was found.

"The left adrenal appeared essentially normal. The right adrenal had been removed at previous surgery. In its place were found scar tissue and tumor recurrence, forming a mass approximately the size of an orange.

"Both kidneys were essentially normal.

"The bladder, uterus, tubes, and ovaries appeared essentially normal.

"All of the lymph nodes along the aorta were enlarged by tumor growth. The largest glands were found in the region of the head of the pancreas and the smallest glands were found near the bifurcation of the aorta. Numerous large mediastinal nodes were present.

"The brain was not examined.

"A section from the tumor mass in the right adrenal (fig. 4) showed a malignant tumor similar to that previously removed from this area and diagnosed as adrenal pheochromoblastoma. The growth was composed of alveolar masses of malignant cells supported by fibrous vascular stroma. The majority of the cells were polyhedral but some had a bipolar appearance. Mitotic figures were seen and some cells presented relatively large nuclei. The cytoplasm in most instances was finely granular. Areas of hemorrhagic infiltration were noted in many places and some necrosis was present.

"Sections showed lymph nodes infiltrated with metastatic tumor similar to that described above.

"A section of liver included metastatic tumor similar in type.

"A section of lungs showed similar appearing tumor.

"A section of the left ventricle showed essentially normal appearing myocardium.

"A section of the spleen showed essentially normal tissue.

"A section of the left adrenal appeared normal.

"No pathological changes were found in the kidneys except for mild albuminous degeneration of the tubule lining cells.

"Sections of the tumor fixed in Zenker solution showed relatively little chromation of the cells. That probably was due to the immaturity of the malignant cells.

"Anatomical diagnosis: Local recurrence of pheochromoblastoma, right adrenal; extensive metastases to regional aortic nodes, liver, mediastinal nodes, lungs, and pleurae; healed surgical scar, right side (right adrenalectomy); gaseous distention of stomach and large bowel. (Dr. G. R. Kerr)."

DISCUSSION

Pheochromocytomas and malignant pheochromocytomas (pheochromoblastomas) must be ruled out in all cases of hypertension, especially in those showing paroxysmal hypertension. When the typical symptom complex is present, the presence of an adrenal medulla tumor is highly probable. More of these tumors will now be reported when we have such valuable aids to diagnosis as the adrenalin antagonist histamine and the adrenergic drug benzodioxane. The diagnosis of medullary tumor in this case was not difficult without perirenal air insufflation. However, as one looks back, it is our belief that this x-ray taken before operation shows signs of chest metastases (fig. 1, *B*). When one considers that less than 200 pheochromocytomas have been reported, and only 9 per cent of these are malignant,[16] a record of these cases is important. In reviewing the literature we have found only one larger. Wells and Boman[17] reported one of 1000 gm. but the one of Borch-Johnsen[18] weighed around 2000 gm. This case again refutes the one time belief that pheochromoblastomas are not associated with paroxysmal hypertension.[19] Rapid metastases and death, as in this case, make a guarded prognosis important. Baumgarten and Cantor consider pheochromocytomas benign anatomically but malignant physiologically. Here we have one that is both anatomically and physiologically malignant. Neither preoperative nor postoperative roentgen therapy was given this patient and its value will no doubt create much discussion. I can only state that if we have a similar case in the future, it will receive postoperative x-ray therapy.

SUMMARY

A brief review of the anatomy, embryology, and physiology of the adrenal medulla is given.

A case of malignant pheochromocytoma or pheochromoblastoma is reported.

An adrenal medullary tumor is to be suspected in all cases of paroxysmal hypertension.

In difficult cases where one cannot produce an attack, it may be induced by the injection of histamine, mecholyl or tetra-ethyl-ammonium chloride.

An extremely valuable diagnostic aid is the injection of adrenergic drugs as benzodioxane or dibenamine.

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[16] MacKeith, R. Adrenal-sympathetic syndrome chromaffin tissue tumor with paroxysmal hypertension Brit Heart J, **6**: 1–12, 1944

[17] Wells, A H and Boman, P G Clinical and pathologic identity of pheochromocytoma Report of a case. J A M A , **109**: 1176–1180, 1937.

[18] Borch-Johnsen, E Paraganglioma gland suprarenal, operated case. Acta Chir. Scandinav , **80**: 171–179, 1937

[19] Chamovitz J and Fanger, H Malignant pheochromocytoma and hypertension (a case report). Am J Clin Path , **19**: 243–251, 1949

[20] Baumgarten, E C and Cantor, M O Pheochromocytoma Ann Surg , **111**: 112–116, 1940

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POLYCYSTIC RENAL DISEASE WITH PARTICULAR REFERENCE TO AUTHOR'S SURGICAL PROCEDURE

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This study of polycystic renal disease was undertaken primarily to obtain comparative data regarding results obtained in 18 cases by an operative procedure described by the author 5 years ago and to compare the results obtained in 18 other patients upon whom conservative treatment was instituted. While the cases were not selected, several patients upon whom we would have operated refused the operation.

No attempt is going to be made to go into any lengthy discussion relative to the historical background excepting as may be necessary to stress some point in the paper. Likewise symptomatology and diagnosis will be dealt with principally as it pertains to this study.

While the etiology of polycystic renal disease has not been settled definitely, we favor the thought of it being the result of renal developmental defects. The origin of the cysts, from our studies seem to give evidence that a congenital defect exists between the secretory and the excretory apparatus.

McKenna and Kampmeier believe that during embryonic life all kidneys possess many cysts but disappear during development, excepting those individuals who for no known reason have a tendency towards development of polycystic disease and in the latter cases the cysts persist. This is quite in contradistinction to Norris and Herman who claim that a definite constriction and segmentation of the nephrons exist, eventually resulting in the isolation of large and small cysts. This they feel follows local obstruction and constriction of a congenital nature.

We are of the firm belief that the condition is hereditary and may involve several members of one family. In this series of 36 cases, a history was obtained in 27 of maternal or paternal polycystic disease and was questionable in 9. Some other member in the family had a similar condition in 23 definitely known cases.

We have been able to trace it in two, three and four generations in some of our cases. Cairns reported on the occurrence of 19 per cent of his cases occurring in 3 generations and Fuller reports on being able to trace it in 4 generations. While rare it has been reported by Reason and Hermandez in twins.

The disease has been reported by Carlson in a congenital solitary kidney, in three polycystic kidneys by Conveleave and Thevenard, and in a bilateral polycystic kidney duplex by Washburn. The association of congenital cysts in other organs has not escaped our notice having occurred twice and has reached the literature by others.

Secondary bone changes (renal hyperparathyroidism) has been reported by Bass and Pakter and others in connection with polycystic degeneration. Bone formation, renal calculi, tuberculosis, renal neoplasm, hydronephrosis, diffuse nephritis and other conditions have been reported in association with polycystic renal degeneration.

We have also noticed in our cases that the condition may occur in various degrees of degeneration. Marked renal damage has been seen at birth and only mild cystic degeneration in adults while in most cases it is quite the reverse. Nevertheless the smallest amount of renal damage is sufficient to show some evidence of renal deficiency and while in some cases it may not impair ones' life, it without a doubt has some detrimental effect. Unfortunately though, when the condition is not too obvious, loss of time in recognition may possibly be detrimental to obtaining some relief that might be afforded to the patient if it were recognized earlier. The most difficult time to recognize the condition is when it is in its early stages, yet sometimes one feels the hopelessness if it were recognized early with the exception of possibly careful observation and some form of early treatment if the occasion arises.

The pathological picture of the disease likewise has not changed except in thought and description.

In our series of cases we have always found the condition to be bilateral yet there are reports of its unilaterality. We believe a case should not be considered unilateral until the other kidney has been exposed either by operation or at autopsy. That the disease is always bilateral unless proved otherwise is well illustrated by the almost invariable appearance of the condition in the opposite kidney after nephrectomy for polycystic disease.

In our present study of a series of 36 cases, the picture was fairly uniform. Bilateral involvement was diagnosed in all of our cases and to date proved by one method or another to be definite in 32. Many cortical cysts ranging in number from hundreds to thousands were found in both kidneys which were always enlarged. The cysts were of various colors, shapes, and sizes. We have observed a pin-point size to some measuring 12 cm. in diameter, removing as much as 300 cc secretion from a single cyst. The contents varied, containing blood, plasma, urea products, albumin, serum, gelatinous material, calcareous deposits, etc. The cysts showed no evidence of communication with each other or with the calyces or pelvis except by rupture. The size of the kidney is dependent upon the number of cysts present; however, both kidneys were not necessarily the same size. On any basis, it is uncommon to see a polycystic kidney that is not larger than normal, reaching sometimes to 4 or 5 times its normal size. Braasch and Schacht report the removal of a polycystic kidney weighing 7,284 gm.

It has been our experience to find the disease at any age but most commonly between the second and fourth decade. The oldest patient with polycystic disease whom we encountered was 60 years, but this is rather unusual, while the youngest was 3½ months.

In our personal series of 36 cases, 20 occurred in the female and 16 in the male.

While the symptoms and signs are not too spectacular, in the 36 personal cases observed by us there were several symptoms and signs which stood out above all others. In the order of their frequency they were as follows:

1) Persistent low specific gravity of the urine (below 1.015)
2) Definite ureteropyelographic changes (bilateral)
3) Pain in upper abdominal or renal regions
4) Definite changes in the blood urea retention and excretory urinary tests
5) Trace of albumin
6) Slight elevation of blood pressure
7) Bilateral palpable masses
8) Secondary anemias
9) Hematuria

Of less importance were symptoms such as headaches, nausea, vomiting, weakness, blurring of vision, itching of skin, hypertension, etc.

From the standpoint of diagnosis, while many factors enter into it, we depended mostly on the persistence of a low specific gravity of the urine with the definite bilateral pyelographic picture. This picture, when definite, reveals an elongated pelvis and calyces with deviation of the ureter to the midline and sometimes a right angulation of the ureter.

In our series, these two findings were always constant in addition to the fact that the pyelographic changes were always bilateral which in our opinion made it more confirmatory.

Sometimes confusion may arise if an associated condition presents itself, such as an accompanying stone, tumor, or polycystic disease in one portion of a double kidney. An associated pyelonephritis or an infected hydronephrosis (Goldstein and Klotz) will also cause the typical picture to be confusing. Aside from infection and an associated hydronephrosis or diffuse nephritis, our series was free from any of the other reported complications.

There are several renal diseases that polycystic disease should be differentiated from and the following ones are the most frequent.

1) Chronic diffuse nephritis.
2) Renal neoplasm.
3) Bilateral infected hydronephrosis.

In chronic diffuse nephritis we have found that while the individual with this disease may present all of the symptoms and signs that an individual with polycystic disease does, rarely, if ever, did we see a case of diffuse nephritis where the kidneys were enlarged. Likewise, in our series of cases of polycystic disease the kidneys were never normal or smaller than normal in size.

The amount of renal functional damage may be the same, but the amount of destruction to the glomeruli and tubules is different. As a rule in chronic nephritis a fair amount of albumin is present while in polycystic disease it is rarely more than a trace. The presence of casts and a large amount of albumin with a low specific gravity of urine as occurs in nephritis at times, are significant when compared to an absence most of the time of casts and only a trace of albumin with a low specific gravity of the urine (below 1.015). In only 2 cases were we able to detect any casts.

Finally, normal ureteropyelograms are found in diffuse nephritis against the characteristic picture already described in polycystic renal disease.

In the question of a renal neoplasm as differentiated from polycystic disease, one is guided considerably by the fact that rarely does renal neoplasm occur bilaterally; therefore, the presence of palpable bilateral renal masses may arouse suspicion against renal neoplasm. While gross hematuria does occur occasionally in polycystic disease, it is one of the most common symptoms in renal neoplasm. Furthermore, should bilateral renal neoplasm exist, certainly the specific gravity of the urine will not be lowered as it is in polycystic disease. As for the pyelographic findings one might become confused because frequently they resemble each other, but in renal neoplasm there is seldom bilaterality of the disease.

In differentiating polycystic disease from bilateral hydronephrosis one should remember that there is no reason for a dilated pelvis in polycystic disease as is found in hydronephrosis unless there is an accompanying bilateral obstruction in the ureters, at the ureteropelvic juncture, or a vesical or intravesical obstruction.

In our series of cases, no obstruction was present; therefore, there was no real hydronephrosis. In 3 cases there was a first degree dilatation of the pelvis. Again, the specific gravity of the urine should not be altered in hydronephrosis nor should there be any separation of the calyces as is seen in the pyelograms of polycystic kidneys.

In our series of 36 cases there never was a question of chronic diffuse nephritis per se being present. As for the presence of renal neoplasm, we were fairly certain of all our cases which were diagnosed as polycystic kidneys.

All of the operative cases were verified at operation and some of the others were autopsied and verified. Of the 18 cases that were not operated on, 12 came to autopsy and the diagnosis verified and one was operated on for another condition, and the diagnosis verified. Three others of these 18 are living and two could not be traced. In other words of the 36 cases studied, the diagnosis was correct to date in 32 cases.

In one case there was a question of hydronephrosis rather than polycystic disease. This patient came to autopsy and the diagnosis of bilateral polycystic renal disease was verified at autopsy.

We depended upon a probable diagnosis on the following:

1) History, most important.
2) Pyelographic picture (bilateral).
3) Specific gravity of the urine, persistently low.
4) Changes in the blood chemistry and excretory functional tests.

One who is quite familiar with the disease is well aware of the hopelessness in most cases whether the treatment is conservative or surgical. Various types of medical and surgical procedures have been advocated. In surgery it has been dilating the ureters and lavaging the kidneys, puncturing of cysts, introduction of sclerosing solutions, suspension of kidneys, nephrotomies, marsupulization, nephrectomy and finally the author's procedure described 15 years ago. Rolnick, Reaves, and Dodson more recently have written on the surgery of polycystic kidney.

In the author's procedure the kidney is exposed and delivered. All the large cysts are evacuated and many of the smaller ones treated similarly. Parts of the walls are excised. As much as 1030 cc fluid has been removed in some cases. The kidney is then split for its whole length down to the calyces and more cysts are exposed and drained. Efforts are made not to open into the calyces or pelvis, otherwise urine will drain for several weeks but is not a serious complication. The open halves of the kidney are then sutured with No. 2 or 3 chromic catgut to the edges of the skin wound, suspending the kidney and leaving it exposed. The sutures are placed through the cortex on each side and then through the muscles, fascia and skin. One, as a rule, does not encounter too much bleeding, but this can be controlled if necessary. A vaseline gauze dressing is applied and the wound kept open as long as possible. A scar will form over the kidney which is directly under the skin. Subsequent punctures are made when necessary through this scar to the kidney without danger of going into the peritoneum or injuring any important structure. See figures 1, 2 and 3.

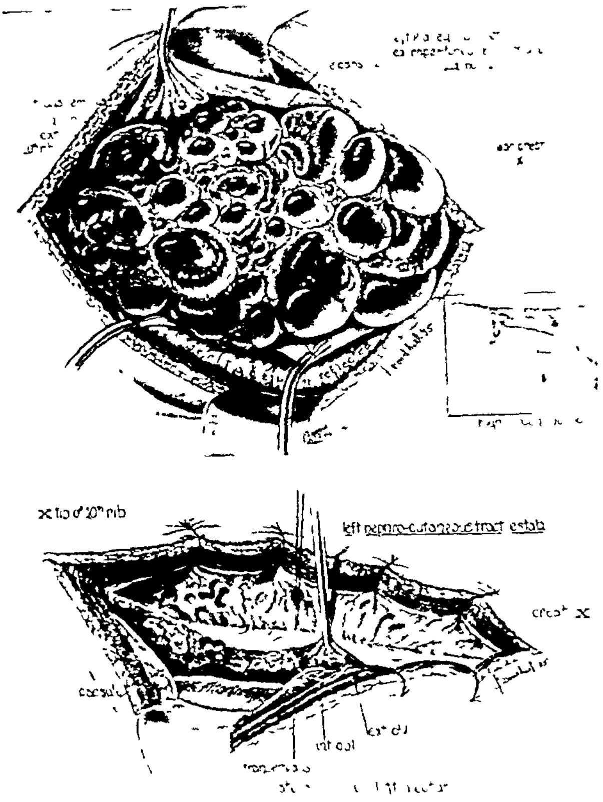
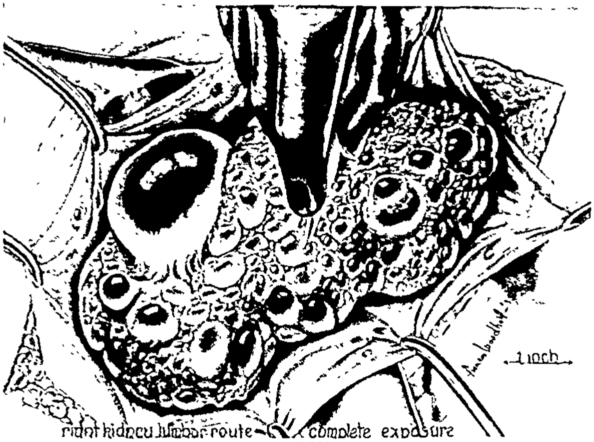
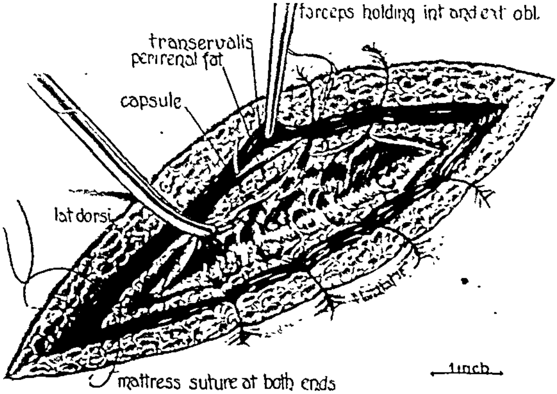


Fig. 1

It is interesting to note that almost the exact procedure as the foregoing was advocated by Herrick in 1921 without any knowledge to us. He carried out some perfusion experiments in cystic kidneys and found that urinary excretion increased after cysts were evacuated. He had not attempted this in the human



right kidney lumbar route—complete exposure


forceps holding int and ext obl.
transervalis
perirenal fat
capsule
lat dorsi
mattress suture at both ends
1 inch

right nephro-cutaneous tract established-lumbar route

Fig. 2

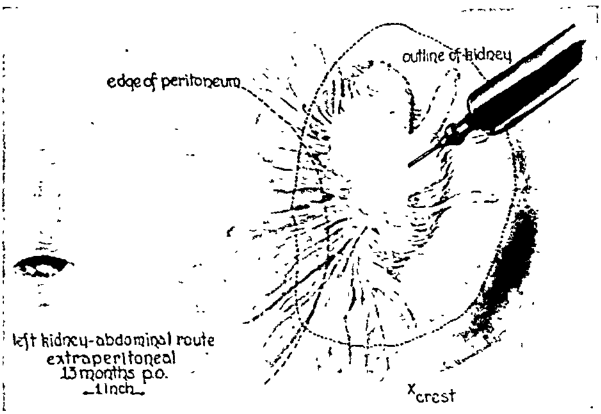


Fig. 3

and the experiments and procedure were dropped until we independently started it in 1934 and 1935. Since then we have performed the operation in 24 cases, but we are only reporting on a recent series. Much has been learned by us since we started. The advanced cases which appear hopeless should not be subjected to operation because it reflects unfavorably on a procedure which at best in these cases is not too good. A number of our cases should not have been attempted but in view of the fact that the patient was in a hopeless situation, we ventured into it and on several occasions brought the patient out of a coma, following which the patient went along fairly comfortable for a while.

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In the treatment of these cases, 18 were operated upon and 18 were given conservative treatment. The latter was not always by choice but by necessity in 7 cases, because the risk was too poor and because of refusal of surgery in 11 cases.

We performed nephrectomy in 2 cases and our indications for this procedure are the following:

1) Marked unilateral infection.
2) Persistent unilateral hematuria.
3) Marked involvement of one kidney with mild involvement of the other kidney.

Our indications for a polycystic renal operation (author's method) is as follows:

1) No results from medical treatment.
2) When renal involvement is not too extensive.
3) Persistent pain or discomfort in one or both kidneys.
4) Gradual rise in blood chemistry.
5) Gradual decrease in excretory urinary tests.
6) Gradual weakness.
7) Persistence of symptoms.
8) Gradual elevation of blood pressure.
9) Pyelographic changes for the worse.
10) For prolongation of life.

An analysis of the operative cases is as follows:

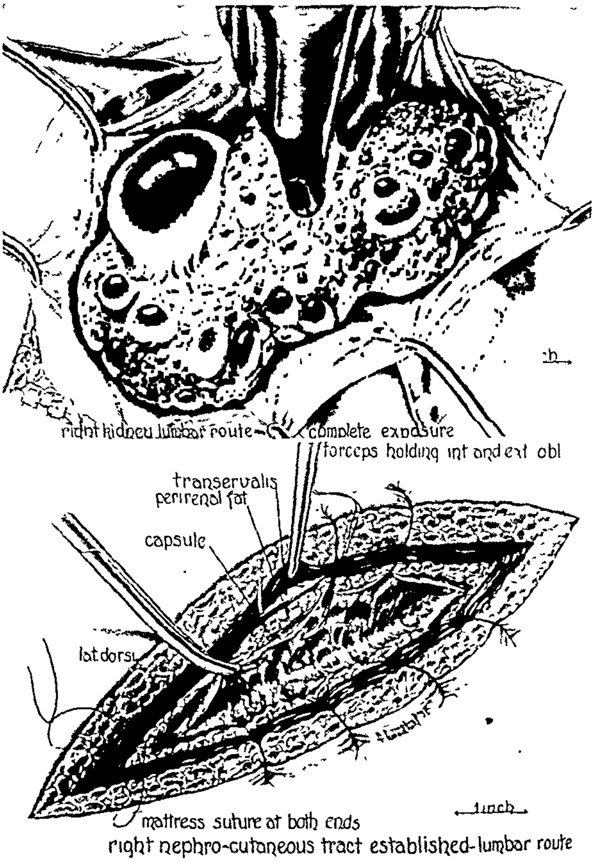
1) In the 18 operative cases, 16 were operated upon by the author's procedure. In these 16 cases, the amount of fluid removed at operation ranged between 75 and 1030 cc with an average of 543 cc. In the past few cases we have not removed more than 500 cc since we have found that removal of more throws the patient into shock. Removal of the secretion permits an improvement in renal function and a decrease of symptoms.

2) Nine had subsequent punctures, while in 9 it was not necessary.

3) The pain disappeared postoperatively in practically all of the cases.

4) There was no definite change in the blood pressure or in the amount of albumin present after the operation.

5) The specific gravity of the urine ranged before the operation between 1.004 and 1.016 with an average of 1.008, while postoperatively, the specific gravity of the urine had the same range but with an average of 1.011. This demonstrated that more solids were passing out in the urine postoperatively.


right kidney lumbar route
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forceps holding int and ext obl
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lat dorsi
1 inch
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right nephro-cutaneous tract established-lumbar route

FIG. 2

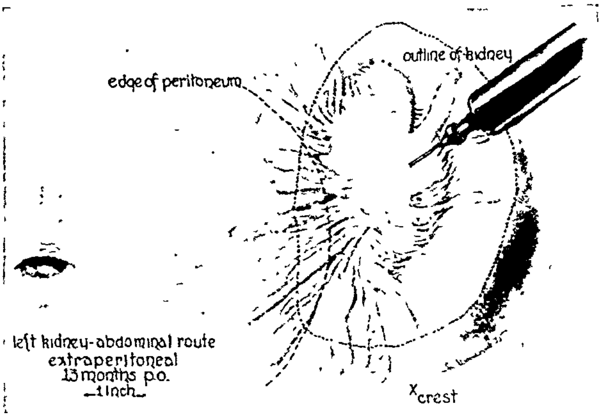

FIG. 3

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6) The blood ureas and excretory functional tests showed definite improvement postoperatively. Some patients prior to operation were in chronic uremia which at sight is unrecognized because they tolerate nonprotein nitrogen retentions (Spencer). The patients who made their exitus did not return to this state until just prior to death.

TABLE 1. *Results in 18 operative cases*
Author's procedure in 16

1. Sex: 7 males and 11 females
2. Age: 24 to 48 years, average 35 years
3. 18 cases
  A. Two nephrectomies
  B. Sixteen, author's procedure
    1. Nine had one kidney operated
    2. Seven had both kidneys operated
  C. Thirteen advanced cases
  Three moderately advanced
4. Subsequent punctures
  A. Nine had from 1 to 5 treatments
  B. Nine, none after original puncture
5. A. Ten dead, all advanced
  B. Eight living, one advanced
    1. Of 10 dead, died, from 2 days to $13\frac{1}{2}$ years after operation, average $4\frac{1}{12}$ years
    2. Of 8 living, 1, 36, 74, 83, 90, 96, 108, 156 months after operation, average $8\frac{1}{2}$ years
6. All 18 cases relieved of pain and generally improved.
7. Of 8 cases living, all but one work and in good condition.

TABLE 2. *Results in 18 nonoperative cases*

1. Sex: 10 males and 8 females
2. Age: $3\frac{1}{2}$ months to 60 years
  average 33 years
3. 18 cases
  A. Eleven dead
  B. Five living
  C. Two, no traces
    1. Of 11 dead, died from 3 months to 5 years after diagnosis, average $1\frac{1}{6}$ years
    2. Of 5 living, 2, 4, 5, 6, and 7 years after diagnosis, average $4\frac{4}{5}$ years
4. Seven of 11 who died, poor risk for surgery
5. Four of 11 who died, refused surgery
6. Five living, refused surgery
7. Two missing, refused surgery

7) Only slight changes in the pyelograms were perceptible postoperatively, yet there was a marked reduction in the size of the kidneys.

8) Seven of the 18 operative cases had both kidneys operated upon.

DISCUSSION

In a discussion of the subject, by referring to tables 1 and 2 and an analysis of the cases, it is apparent that we are dealing with a devastating disease. At best there is no hope for a cure up to the present time, but every effort must be made to relieve by making an early diagnosis.

Pain and discomfort in most cases are troublesome symptoms and should be relieved if possible without subjecting the patient to any unnecessary procedures. Other subjective and objective symptoms must be dealt with in the best possible manner.

Certainly from an analysis of the cases which were not subjected to surgery, one readily realizes the futility.

Of the 11 known cases of death in the nonoperative group, the longest period in which a patient remained alive was 5 years, with an average of $1\frac{1}{6}$ years. In this same group, of the 5 who are living, the longest period to date is 7 years with an average of $4\frac{4}{5}$ years. It might be argued that had any of the 11 who died been subjected to surgery before the patients became moribund, the results would have been different. Certainly they could not have been any worse. By comparing these cases with those with the same condition who were subjected to surgery, one would say that the results were somewhat better among the operative cases. One lived as long as $13\frac{1}{2}$ years and the entire group averaged $4\frac{1}{12}$ years of life, an average of almost four times as long, plus the comfort they had for awhile following the operation. Of the 8 living, one lived as long as 13 years with an average of all of $8\frac{1}{2}$ years, practically twice as long as those who lived without surgical interference, plus again the comfort they are having for awhile after the operation. This average span of life will certainly be increased, because one of these patients has recently been operated upon and is doing nicely. Three of the patients who died very shortly after the operation never should have been operated upon because of their poor condition. They were in coma at the time. The other seven were so far advanced that they likely would be excluded for operation in the next series of cases. Of the five who are living without surgical procedure only two have been able to occupy their time partly and one happens to be a physician. Of the eight living after the surgical procedure, all but one are engaged in their previous occupations.

CONCLUSIONS

Data have been obtained in an equal number of cases relative to the merits of treating polycystic renal disease by the conservative nonoperative and the radical operative method.

The average duration of life is less when the disease is treated conservatively.

The average duration of life in polycystic renal disease is twice as long (after a diagnosis is made) if treated surgically than otherwise.

In our hands, the author's operation has proved the best surgical procedure.

The patients who were subjected only to a unilateral operation had a definite decrease in size in the unoperative kidney as well as in the operative one.

This surgical procedure improves the general condition of the patient by decreasing the severity of the symptoms, reducing the size of the kidneys, and improving the renal function.

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REFERENCES

Bass, M. H. and Pakter, J.: J. Mt. Sinai Hospital, **4:** 882, 1938.
Braasch, W. F. and Schacht, F. W.: Trans. Amer. Assoc. Genito-Urin. Surg., **25:** 71, 1932.
Cairns, H. W. B.: Quart. J. Med., **18:** 359–392, 1925.
Carlson, H. E.: J. Urol., **55:** 443, 1946.
Conveleave, R. and Thevenard, P.: Bull. Soc. Franc. d'urol., pp. 106–108, Nov. 1940.
Dodson, A. I.: J. Urol., **57:** 209, 1947.
Fuller, C. J.: Quart. J. Med., **22:** 567, 1929.
Goldstein, A. E.: J. Urol., **34:** 536, 1935.
Goldstein, A. E. and Klotz, B.: Surgery, **6:** 730, 1939.
Hermandez, I. M.: Sem. Med., **2:** 1430, 1930.
Herrick, F. C.: Ohio State Med. J., **17:** 89, 1921.
McKenna, C. M. and Kampmeier, O. F.: Surg. Gynec. & Obst., **36:** 208, 1923.
Norris, F. R. and Herman, L.: Tr. Am. Assoc. Genito-Urin. Surg., **31:** 41, 1938.
Reason, C. H.: Canad. M. A. J., **29:** 612, 1933.
Reaves, J. U.: South. Surg., **11:** 254, 1942.
Rolnick, H. C.: J. Urol., **47:** 648, 1942.
Spencer, H. R.: South. Med. J., **30:** 524, 1937.
Washburn, F. H.: J. Urol., **24:** 199, 1930.

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TRANSLUMBAR NEPHROCOLOPEXY

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The fact that a few of the cases operated on by us for nephroptosis returned complaining that they were not free of their symptoms, prompted us to carry out a more complete study in all these cases.

In all suspected case of nephroptosis, we take a minute history; and, besides the routine urological examination, we do a gastro-intestinal series and barium enemas.

We have observed that these patients are nervous individuals and their usual complaints are: loss of weight, gastric distress, constipation, and loss of appetite, besides the cardinal symptom of nephralgia.

In this study we observed that nephroptosis is not uncommonly associated with enteroptosis (Glenard's disease) or a displacement downward of the colon, particularly in women, in whom these conditions are more prevalent.

This observation prompted us to devise the operation, translumbar nephrocolopexy. The technique is the usual lumbar incision and the Lowsley ribbon gut technique is carried out for the nephropexy (figs. 1 to 5). Following this procedure, the peritoneum is opened, the appendix is removed, the anterior band of the ascending colon is identified and is followed upwards the distance of 6 to 8 inches to the point where it turns, which corresponds with the hepatic flexure of the colon (fig. 6).

The anterior band at the level of the hepatic angle is sutured, using State suture material, to the superior angle of the peritoneal wound and to the ribbon gut at the inferior pole of the kidney.

In the past 4 years, we have performed this operation on 67 cases, all of them women between the ages of 20 and 45 years, and weighing between 80 and 110 pounds. All were improved clinically, and the gain in weight ranged between 11 and 45 pounds.

I wish to present for your consideration some illustrations of these cases, before and after the operation (figs. 7 to 12).

SUMMARY

It has been shown by the postoperative study presented that the kidney and hepatic angle of the colon have been restored to their normal anatomical position by the technique of translumbar nephrocolopexy.

The observation has been that patients' general health improves as shown by the gain in weight of 11 to 45 pounds, and the fact that these patients have been free of symptoms while we have had them under observation.

Coincidentally, it has been shown that nephroptosis is frequently associated with a displaced colon: and that this condition is more prevalent in women.

Read at annual meeting, Southeastern Section, American Urological Association, Gulfport, Miss., February 3, 1950.

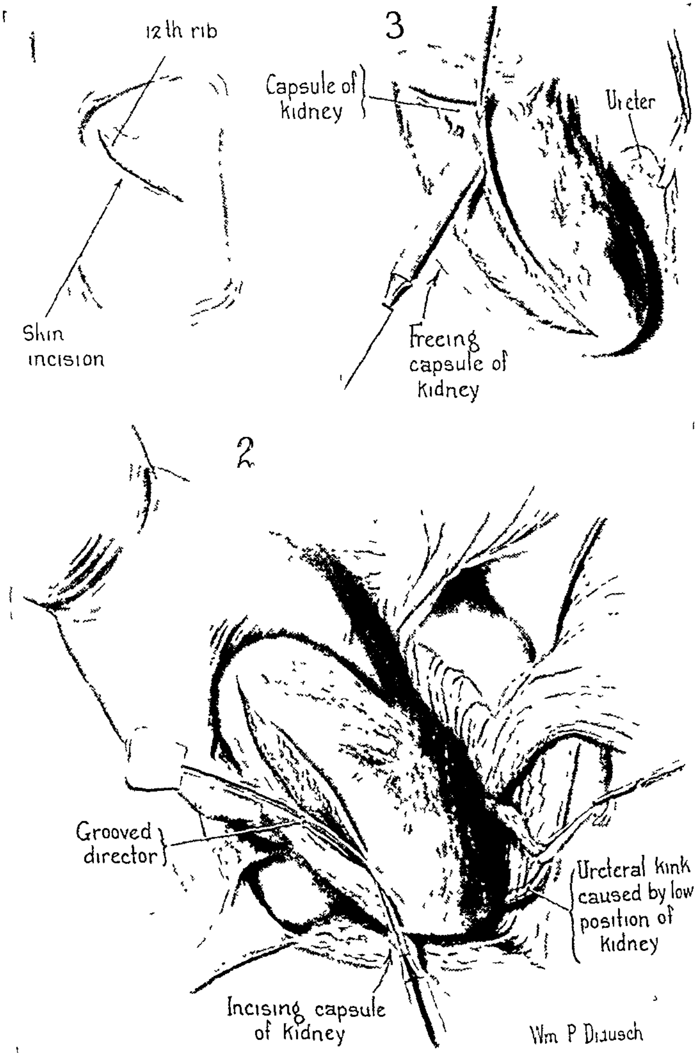
1
12th rib
Skin incision
3
Capsule of kidney
Ureter
Freeing capsule of kidney
2
Grooved director
Ureteral kink caused by low position of kidney
Incising capsule of Kidney
Wm P Didusch

FIG. 1. Nephropexy using chromicized ribbon gut. *1*, Lumbar skin incision. *2*, Kidney has been mobilized and delivered. Incising fibrous capsule of kidney. *3*, Freeing capsule so as to expose about one sixth of renal surface. (From Lowsley and Kirwin: Clinical Urology. Baltimore: Williams & Wilkins, 1944.)

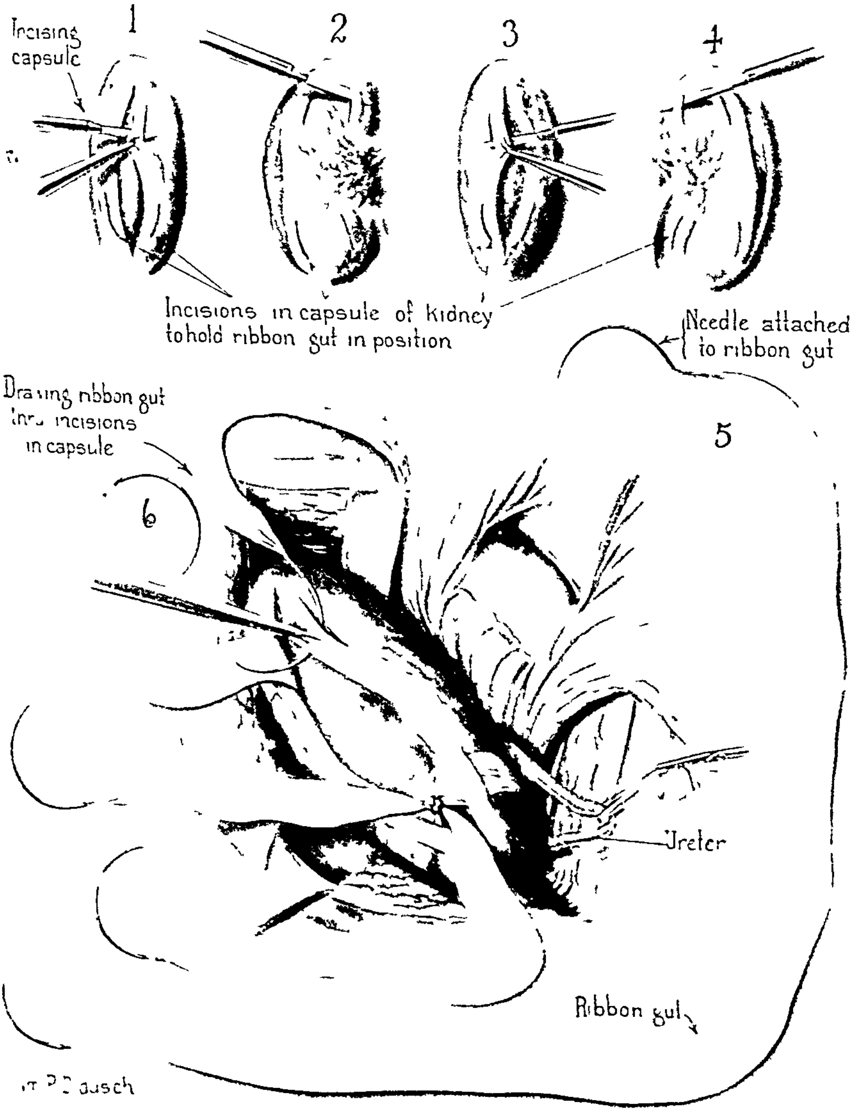
1
2
3
4
Incising capsule
Incisions in capsule of kidney to hold ribbon gut in position
Needle attached to ribbon gut
5
Drawing ribbon gut thru incisions in capsule
6
Ureter
Ribbon gut
Bausch

Fig 2 *1* to *4*, Making incisions in fibrous capsule, at upper and lower poles, to hold ribbon gut in position *5*, Chromic ribbon gut with needle attached *6*, Ribbon gut in position about lower pole Drawing gut through incisions in upper pole (From Lowsley and Kirwin)

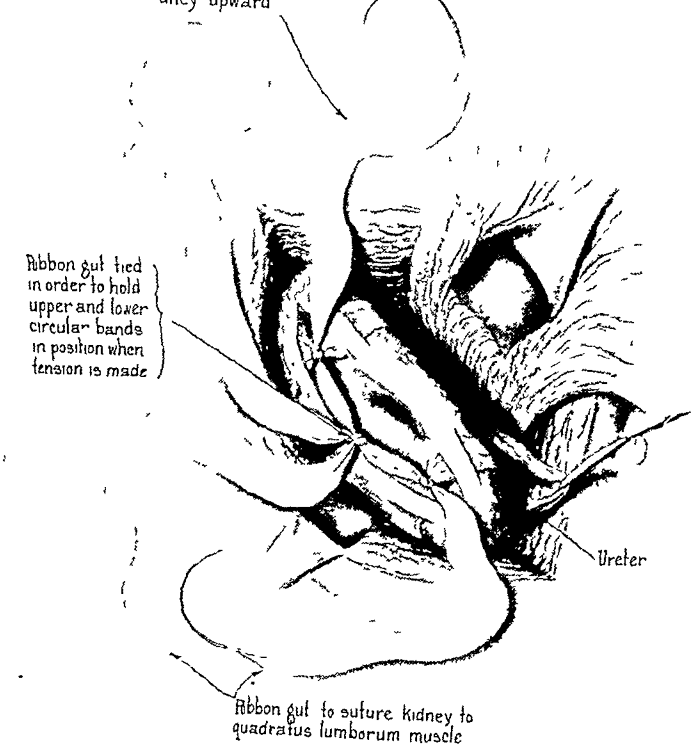
ney upward
Ribbon gut tied in order to hold upper and lower circular bands in position when tension is made
Ureter
Ribbon gut to suture kidney to quadratus lumborum muscle

FIG. 3. Showing ribbon gut in position about two poles of kidney. One of strand about upper pole is tied to free end of strand about lower pole to hold two slings firmly in position when tension is made. (From Lowsley and Kirwin)

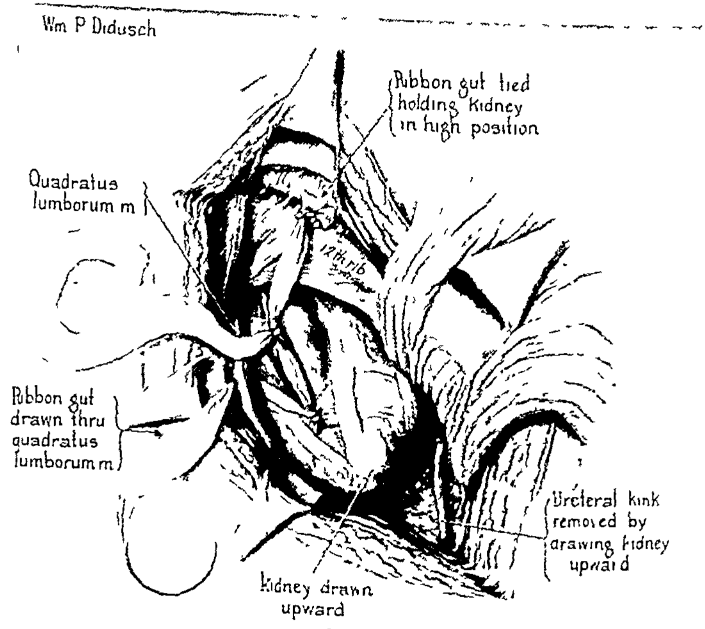
Wm P Didusch
Ribbon gut tied holding kidney in high position
Quadratus lumborum m
12th rib
Ribbon gut drawn thru quadratus lumborum m
Ureteral kink removed by drawing kidney upward
Kidney drawn upward

FIG. 4. Needle studded end of upper sling of ribbon gut has been inserted through twelfth intercostal space, drawing kidney with its partly denuded cortex upward; it has then been firmly tied, so that the kidney is held in high position. Needle-studded end of lower sling is being drawn through quadratus lumborum muscle (From Lowsley and Kirwin)

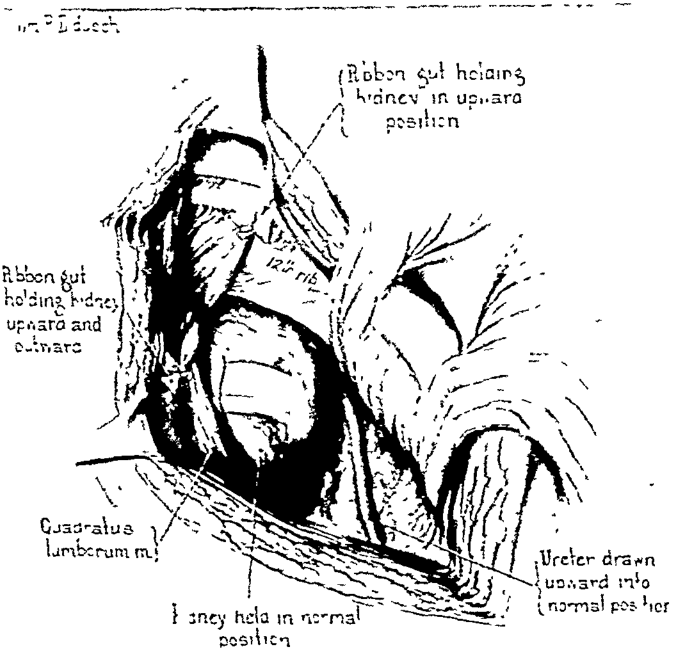
Wm P Didusch
Ribbon gut holding kidney in upward position
12th rib
Ribbon gut holding kidney upward and outward
Quadratus lumborum m.
Kidney held in normal position
Ureter drawn upward into normal position

Fig. 5. Operation completed Kidney drawn upward and outward, with urete free and straight. (From Lowsley and Kirwin.)

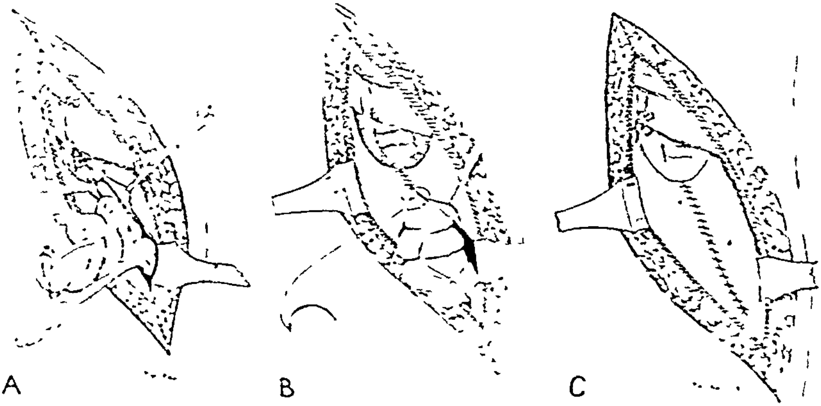

Fig 6 *A* peritoneum is opened and appendix removed, *B*, anterior band of ascending colon is followed to hepatic flexure and sutured to superior angle of peritoneal wound and to ribbon gut at inferior pole of kidney, *C*, nephrocolopexy has been ended

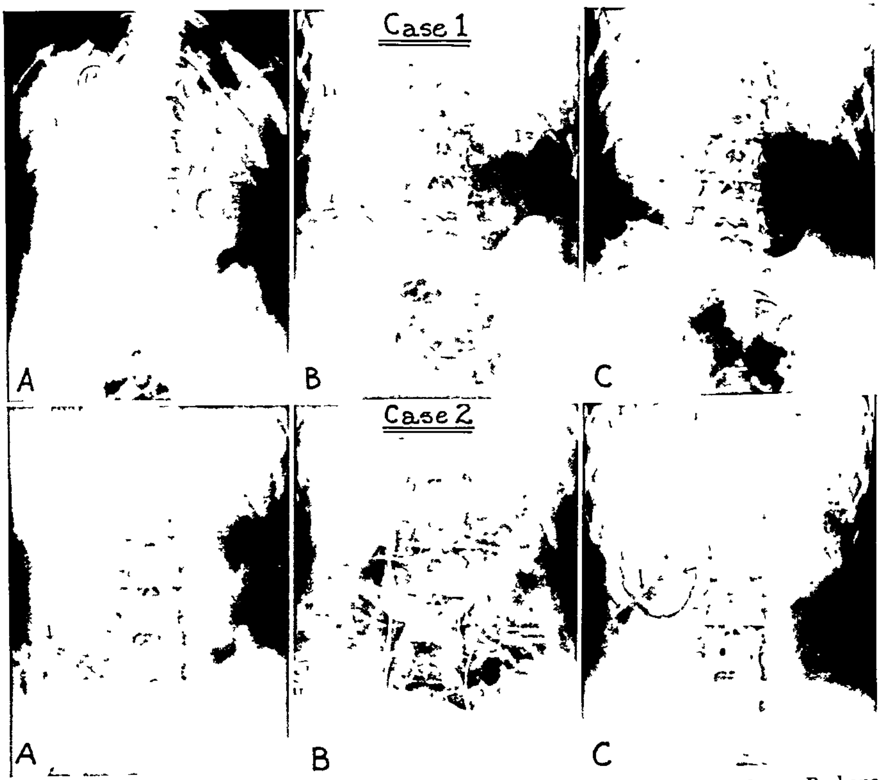

Fig. 7. Case 1. *A*, preoperative vertical film. Marked ptosis of right kidney. *B*, hepatic angle of colon in iliac fossa. *C*, postoperative film, vertical position. Right kidney of hepatic angle of colon in normal position.

Case 2. *A*, preoperative vertical film. Right renal pelvis at level of body of fourth lumbar vertebra. Hepatic angle of colon, full of gas, over iliac crest. *B* and *C*, postoperative films, vertical position. Right kidney in normal position. Hepatic angle of colon, full of gas, over lower third of anterior aspect of kidney.

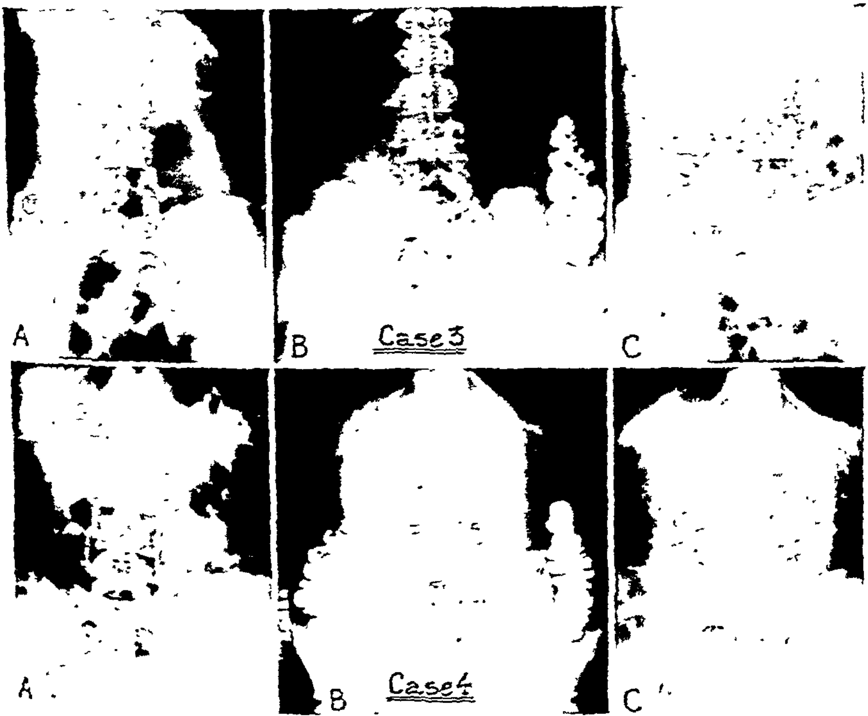

FIG. 8. Case 3. *A*, preoperative vertical film. Mild ptosis of right kidney. *B*, hepatic angle of colon under right iliac crest. *C*, postoperative film, vertical position. Right renal pelvis in normal position, but not so hepatic angle of colon, which was fixed a little low during colopexy.

Case 4. *A*, preoperative vertical film. Lower pole of kidney just above iliac crest. *B*, hepatic angle of colon just above iliac crest. *C*, postoperative film, vertical position. Right kidney and hepatic angle of colon both in normal position.

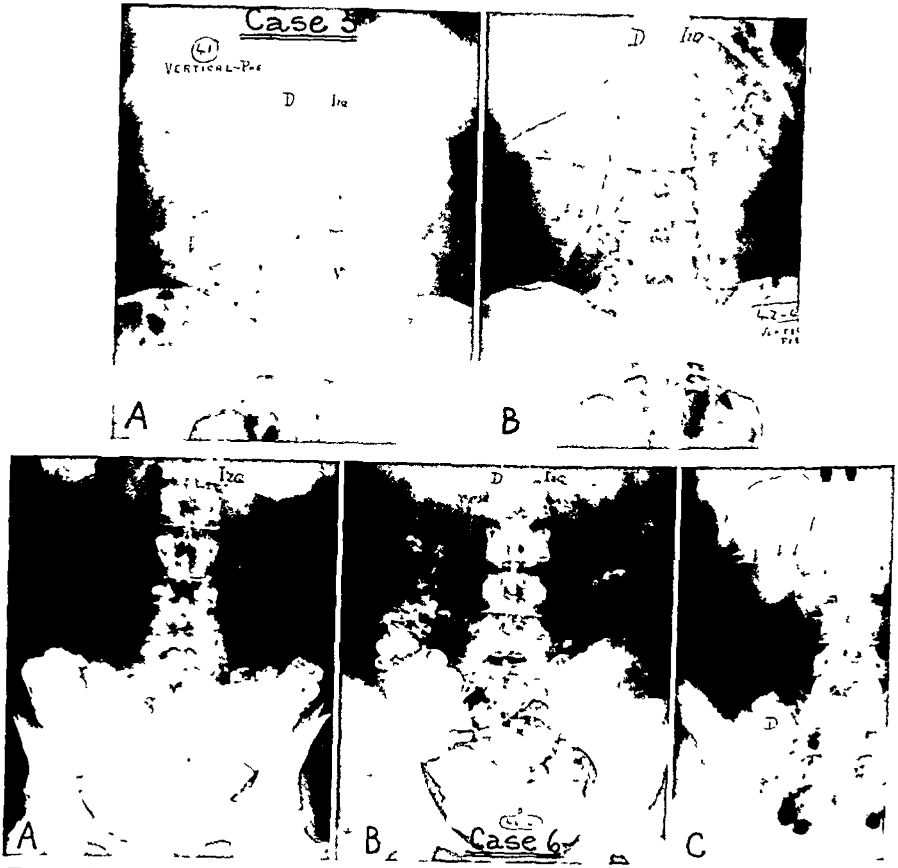

FIG. 9. Case 5. *A*, preoperative vertical film. Marked ptosis of right kidney. Hepatic angle of colon above iliac crest. *B*, postoperative film, vertical position. Right kidney and hepatic angle of colon in normal position.

Case 6. *A*, preoperative vertical film Inferior pole of right renal silhouette touching iliac crest. Transverse colon and its hepatic angle, both full of barium, very ptotic at bottom of pelvic vone *B*, postoperative vertical film. Transverse colon and its hepatic angle quite elevated, especially at angle, which is amply in contact with rear aspect of kidney. *C*, no change in film taken 6 months later.

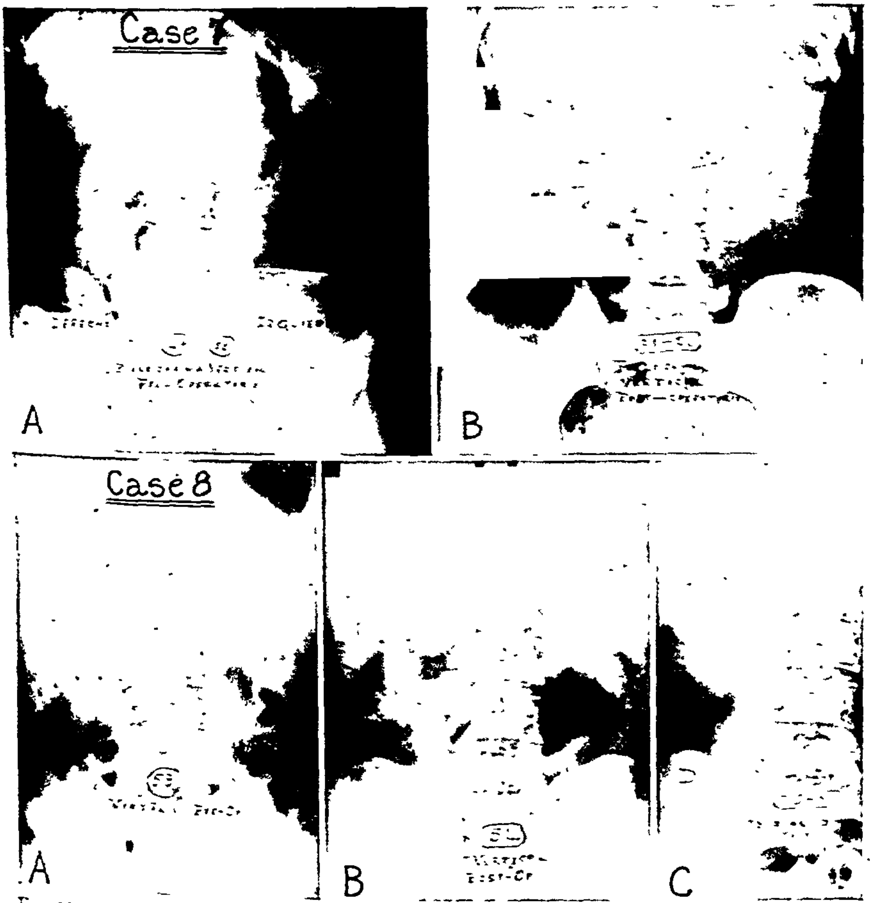

Fig. 10. Case 7. *A*, preoperative vertical film. Marked ptosis of right kidney and hepatic angle of colon. *B*, postoperative film, vertical position. Right kidney and its hepatic angle in normal position.

Case 8. *A*, preoperative vertical film. Mild ptosis of right kidney. *B*, postoperative film, vertical position. Right kidney and hepatic angle considerably raised. *C*, film taken 23 days after discharge of patient. Colon and right kidney still in normal position.

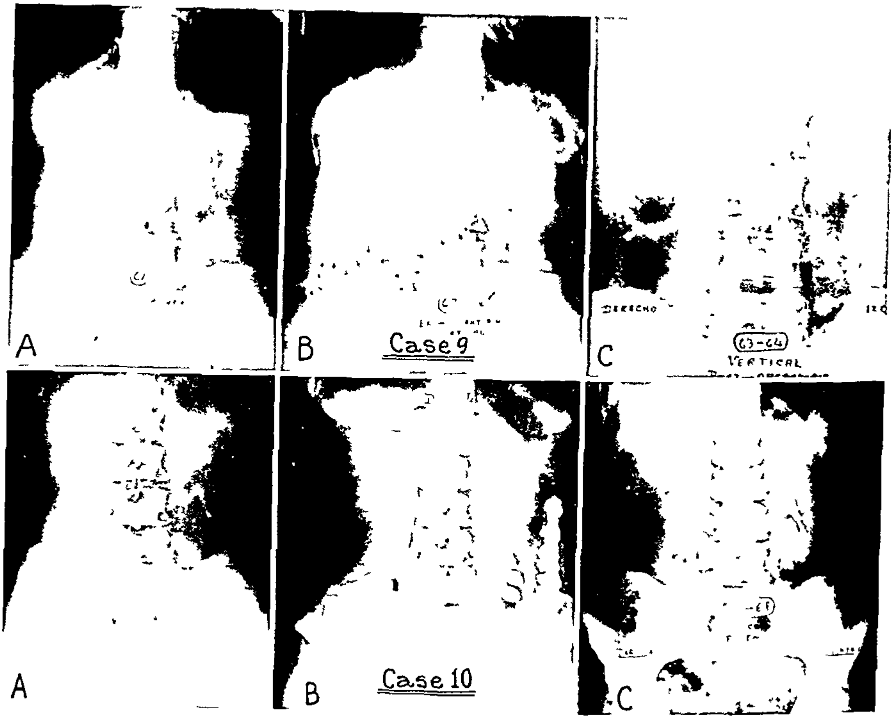

FIG. 11. Case 9. *A*, preoperative vertical film. Right renal pelvis at level of body of fourth lumbar vertebra *B*, lower pole of right kidney at iliac crest; hepatic angle of colon in right iliac fossa. *C*, postoperative film, vertical position. Right kidney in normal position. Hepatic angle of colon above anterior aspect of kidney.

Case 10. *A*, preoperative vertical film. Right renal pelvis, slightly ptotic, at level of body of third lumbar vertebra. On left side, marked ptosis of kidney. Transverse colon (indicated by arrows) on floor of pelvis. *B*, film taken 10 hours after ingestion of barium showing same result. *C*, postoperative film, vertical position. Right kidney only slightly raised. Hepatic angle of colon correctly sutured to middle section of anterior aspect of kidney.

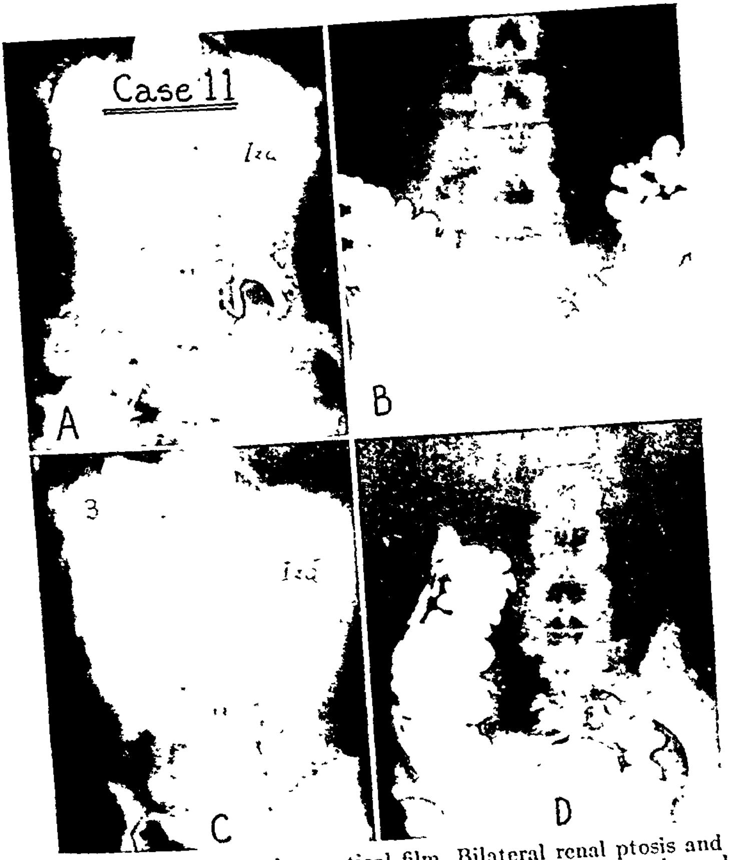

FIG. 12. Case 11. *A*, preoperative vertical film. Bilateral renal ptosis and kink of left ureter. *B*, transverse colon, hammock fashion, on floor of pelvis. Hepatic angle at level of iliac crest together with kidney. *C*, postoperative vertical film. Good result, right kidney being fixed high at level of third lumbar vertebra. *D*, hepatic angle of colon, high above iliac crest, fixed at middle section of anterior aspect of right kidney.

REFERENCES

BANET, V Clinica y Terapéutica Quirúgicas Havana, 1938, pp 123-131.
DODSON, A I Urological Surgery St Louis C V Mosby Co , 1944, pp 239-240
GAZZOLO, J J Trat de las Enf Génitourinarias, 1944, pp 948-960
HERMAN, L The Practice of Urology Philadelphia W B Saunders Co , 1945, pp 179-18
LOWSLEY, O S AND KIRWIN, T J Clinical Urology Baltimore Williams & Wilkins, 194
vol 1, pp 141-149, vol 2, pp 339-472, 682
MARION, G Técnica Quirúrgica 1932, vol 2, pp 188-193
PELOUZE, P S Office Urology Philadelphia W B Saunders Co , 1941, pp 518-520

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SEVERE HEMATURIA WITH ASSOCIATED MINUTE PAPILLOMA OF RENAL PELVIS: CASE REPORT

FREDERICK M. JACOBS AND L. H. BROWN

In the majority of cases of hematuria investigation by modern diagnostic methods reveals positive causative pathology. However, in about 4 per cent[1] of these cases the lesion is not found and the case, usually one of renal hematuria, must be classified as essential or idiopathic. With increasing knowledge and more careful studies a large portion of this group will eventually be assigned to their proper etiological categories.

Many obscure causes of renal hematuria have been found. It has been postulated that many cases of essential hematuria are due to localized nephritis,[2] but Randall[3] believed that most cases were due primarily to obstruction, either venous or urinary on the basis of extrinsic causes such as aberrant vessels or abnormal kidney position, the nephritis being secondary to congestion, hemorrhage and irritation following such obstruction. Microscopic vascular dilatations in the walls of the renal pelvis or on the renal papillae have been considered a probable cause by numerous authors, but in 1944 Rottino and Mohan[4] found only 50 cases in the literature. In 1948 Chenery and Benson[5] were able to accept only 45 proved cases and Riley and Swann[6] in 13,219 consecutive autopsies found no case of renal angioma. However, that many such lesions may remain unidentified is attested to by Rappoport,[7] who was able to find only 1 case of hemangioma of the renal pelvis diagnosed preoperatively. Even postoperatively diagnosis is often made only after microscopic examination[8] even though hematuria may have been severe.

Instances of familial renal hematuria have been reported. Guthrie[9] found episodes of gross hematuria in 12 relatives. Aitken[10] reported 11 cases in five generations, and Atlee[11] reported 3 cases. In these cases blood casts were present in varying numbers at all times and gross hematuria occurred in paroxysms, but in most cases no symptoms of renal insufficiency were noted.

The present case is interesting not only because the cause of hematuria was obscure but also because of its severity and apparent familial nature.

CASE REPORT

A 52 year old white man had noted recurrent hematuria since childhood. These episodes were said to follow unusual physical exertion, were asymptomatic except for mild pain in the right costovertebral angle immediately preceding onset of hematuria, and varied in duration from 1 to 3 weeks. Examination by a number of urologists over a period of years showed that the bloody urine always came from the right ureteral orifice and was never observed spurting from the left ureteral orifice.

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[1] Cahill, G. F. J. Urol., 47: 224, 1942.

[2] Herman, L. The Practice of Urology. Philadelphia and London: W. B. Saunders Co., 1943.

[3] Randall, A. J. A. M. A., 60: 10, 1913.

[4] Rottino, A. J. Urol., 51: 601, 1944.

[5] Chenery, A. J. and Benson, A. H. J. Urol., 59: 164, 1948.

[6] Riley, A. and Swann, W. J. Jr.: Urol. and Cutan. Rev., 45: 377, 1941.

[7] Rappoport, A. E. Arch. Path., 40: 84, 1945.

[8] Webb Johnson, A. and Warwick, W. T.: Brit. J. Urol., 13: 127, 1941.

[9] Guthrie, L. G. Lancet, 1: 1243, 1902.

[10] Aitken, J. Lancet, 2: 444, 1909.

[11] Quoted from Aitken.[10]

In June 1947, shaking chills and fever of 1 day's duration were noted accompanied by dull pain in the costovertebral angles bilaterally and followed by hematuria, dysuria, and frequency. One week following the onset of symptoms the patient was hospitalized. Physical findings at this time were essentially negative. The urine contained many white blood cells and red cells. Long bone series revealed no pathological changes, and complete blood count and blood nonprotein nitrogen were within normal limits. Excretory and retrograde urography showed no evidence of disease, and cystoscopy revealed no bleeding from the ureteral orifices. The symptoms subsided and the urine cleared within 1 week after admission. The patient was discharged without discovery of the cause of hematuria.

Following heavy lifting 11 days prior to the present admission the patient noted onset of slight pain in both flanks followed by gross hematuria which persisted until admission on December 31, 1947. Between episodes of hematuria the patient remained asymptomatic. No persistent or recurring hemorrhages other than hematuria had been noted.

The patient's father, grandfather and two brothers had suffered similar episodes of gross hematuria without other symptoms suggestive of renal disease. Three brothers and 1 sister were not afflicted. The grandfather and father of the patient had many severe attacks beginning in childhood and often severe enough to cause noticeable weakness. The grandfather lived to be 85 and the father to be 77, and in neither did hematuria persist after the middle fifties. The two brothers suffered less severely, one to date having noted only 3 brief episodes of hematuria and the other brother only one episode. These cases have all been characterized by episodes of hematuria appearing suddenly following severe physical effort of some type, by the lack of other urinary symptoms, the complete absence of symptoms between attacks, and by the absence of other spontaneous hemorrhage.

Physical examination revealed a slightly undernourished white man who did not appear acutely ill. A small telangiectatic area was present inside the lower lip and several similar areas 1–2 mm. in diameter were present on the chest. The blood pressure was 152/98, and a grade 2 systolic murmur was present over the cardiac apex. The left lateral lobe of the prostate was slightly enlarged and prostatic secretions contained many white cells. Increased capillary fragility was present as evidenced by a Gothlin index of 22.

The urine was red, opaque, and loaded with red blood cells. Urine culture showed Aerobacter aerogenes and Pseudomonas aeruginosa. Two 24 hour urine specimens were cultured but no acid fast organisms found. The blood contained 5,400,000 red cells per cubic millimeter and 16.1 gm. of hemoglobin, but was otherwise not remarkable. Blood studies revealed no hemorrhagic tendencies, the prothrombin time, bleeding time, clot retraction time, coagulation time and platelet count being well within normal limits. The blood nonprotein nitrogen was 34 mg. per cent and Kolmer and Kahn tests were negative.

Shortly following admission, cystoscopy revealed blood spurting from the right ureteral orifice, and clear urine from the left. Retrograde pyelograms showed no pathological changes. Complete bed rest and sedation with morphine and barbiturates had no apparent effect on the hematuria, the centrifuged fresh urine specimens containing about one-thirtieth red blood cells by volume. Vitamin supplements with excess of vitamin K, vitamin C, and rutin also were ineffective. On January 23 the right renal pelvis was lavaged with thrombin without any noticeable change in hematuria. Differential renal function test with indigo carmine showed normal excretion bilaterally. As hematuria continued, hemoglobin fell to 13.6 gm. and erythrocytes to 4.55 million. On February 3 right nephrectomy was performed. Hematuria disappeared following surgery and the patient remained asymptomatic. Six months since this procedure the patient has shown no evidence of hematuria.

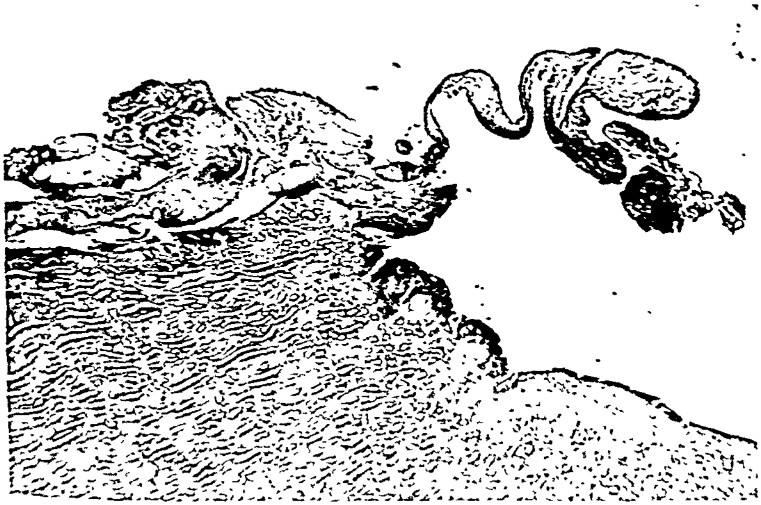

Fig. 1. Small papilloma attached by narrow vascular stalk to pelvic lining

Pathological report (Dr. D. J. Greiner): "Specimen consists of a kidney measuring 12 by 8 by 2 cm. The capsule is dull grey in color, transparent and strips with ease. On the posterior surface of the kidney close to the upper pole, there is a dark reddish brown area measuring 1 by ½ cm. The subcapsular surface is smooth with no fetal lobulation. The cortex is red in color and surrounds a dark red medulla. A small cystic structure ½ cm. in diameter is present in the medulla. There is a normal amount of peripelvic fat present. The pelvis shows nothing of note. The uppermost papilla shows an irregular dark brown depression at its apex. The succeeding lower papilla shows a minute brownish projection at its apex."

Sections were taken through ecchymotic area, through the upper papilla for serial section, through the next two lower papillae for serial section, and through the cyst wall. "Several serial sections of kidney are examined which show recent intracapsular hemorrhage. The glomeruli show mild, generalized atrophic changes with varying degrees of hyalinization. The remainder of the nephron shows nothber of urologists over a period of years showed that the bloody urine always came from the right ureteral orifice and was never observed spurting from the left ureteral orifice.

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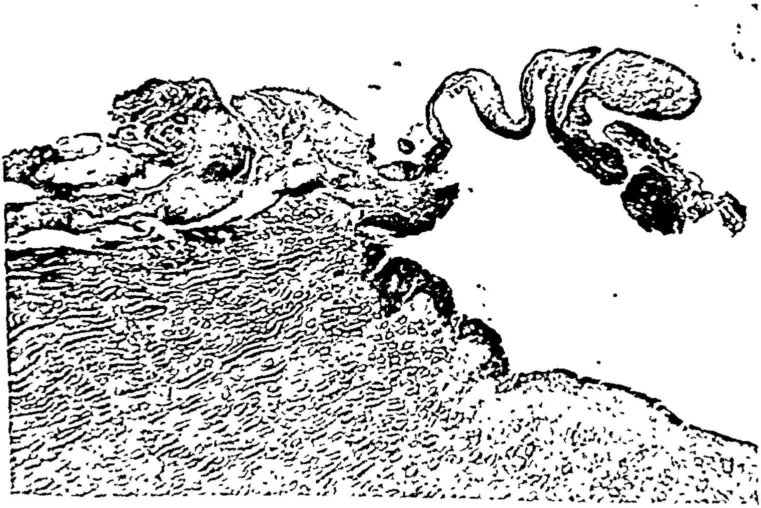

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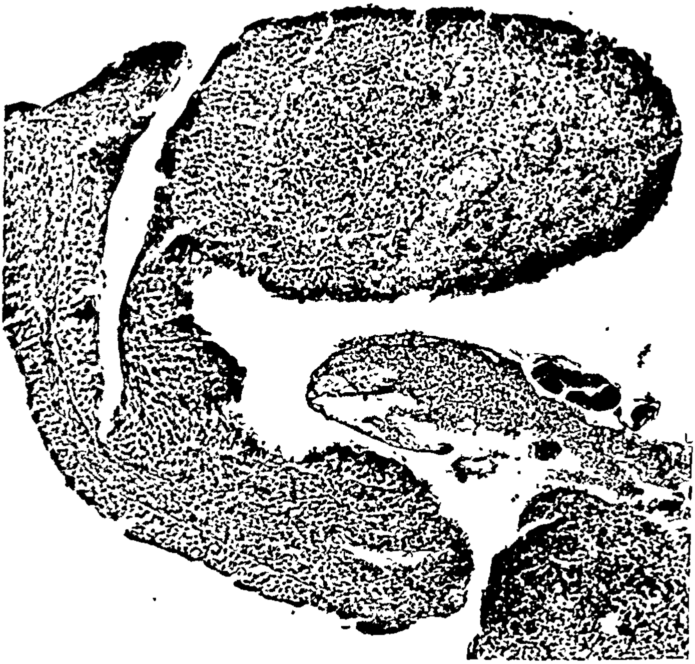

FIG. 2. Same as figure 1, showing thin epithelial layer over surface and dilated thin walled vessels, largest of which reaches surface of papilloma at a point where mucosa is denuded. Both acute and chronic inflammatory cells are present in stroma. Fresh clotted blood is seen between papillary projections.

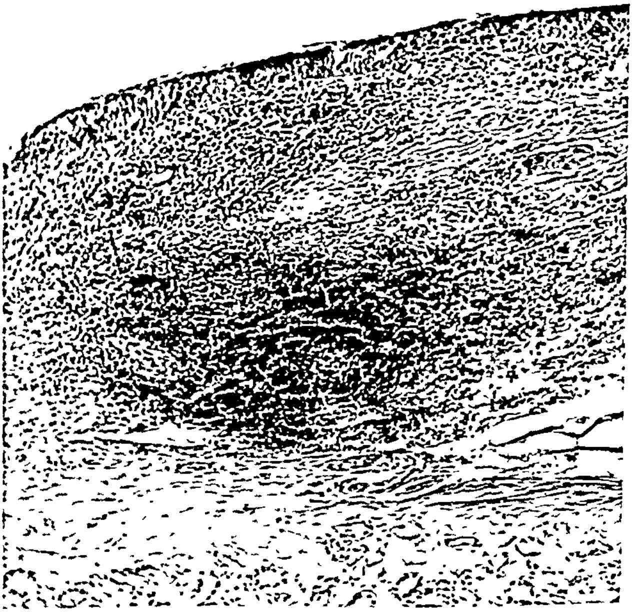

FIG. 3. Photomicrograph to demonstrate chronic inflammatory infiltration beneath pelvic epithelium in region of papilloma

ing of note, but in the collecting tubules there are found several renal calculi of varying color. The larger vessels show moderate thickening of their walls. In one area of the renal pelvis, many small thick walled vessels can be identified, and extending away from these vessels is moderate recent hemorrhage. Protruding into the renal pelvis is a small papillomatous growth between the fronds of which is mild recent hemorrhage. At the base of the papilloma there is fibrosis and hyalinization of the papilla with mild round cell infiltration. Diagnosis: Renal papilloma, renal calculi, chronic inflammation, hemorrhage recent, mild arteriosclerotic kidney."

Three of the patient's brothers, 2 with a history of hematuria and 1 without such a history, were examined and found to have telangiectatic areas on the trunk but none on the face or fingers. Of the 2 brothers suffering from hematuria one had a Gothlin index of 16. The other afflicted brother and one who had never noted hematuria had normal Gothlin indices.

DISCUSSION

The accompanying photomicrographs (figs. 1, 2, 3) show the essential pathological findings.

Unlike previously reported cases of familial hematuria, the urine in the present case was free of blood between episodes and no casts were seen during the most profuse hematuria. On this basis hemorrhage was thought to originate within the renal pelvis from some lesion too small to be diagnosed by pyelography. In view of the cutaneous telangiectases and familial history, hemorrhagic hereditary telangiectasia was considered even though hematuria on the basis of hereditary telangiectasia has been reported in only seven instances.[12]

Conservative methods were continued for a long period in order to avoid the sacrifice of a functionally active kidney. Vitamin therapy, lavage of the renal pelvis, sedation and bed rest were given reasonable trial without success. As an increased capillary fragility had been noted, therapy with rutin as suggested by Zfass and Shanno and Griffith[13] was instituted, but 3 days later, because of continuing severe hematuria, right nephrectomy was performed.

Pathological findings in the excised kidney were minimal. While the minute papilloma could have been the origin of the profuse hemorrhage it is difficult to account for the familial history on this basis, and it is unlikely that the papilloma had been present since childhood. The tubular calculi were not considered to be of importance because of their high incidence in patients free of clinical renal disease.[14]

SUMMARY

A case of intermittent, severe, familial, renal hematuria of long duration is presented in which cutaneous telangiectases were present and in which a minute papilloma in the excised kidney was the chief pathological finding.

27 S. Reese St., Memphis, Tenn.

[12] Voyles, G. Q. and Ritchey, J. O.: Ann. Int. Med., 22: 730, 1945.

[13] Zfass, H. S.: Virginia M. Monthly 74: 56, 1947.
Shanno, R. L.: Am. J. M. Sc., 211: 539, 1946.
Griffith, J. Q., Couch, J. F. and Lindauer, M. A.: Proc. Soc. Exper. Biol. & Med., 55: 228, 1944.

[14] Anderson, L. and McDonald, J. R.: Surg., Gynec. & Obst., 82: 275, 1946.

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RENAL TUMORS: PATHOLOGY AND PROGNOSIS IN 295 CASES

N. C. FOOT, G. A. HUMPHREYS AND W. F. WHITMORE

From the Department of Surgery (Urology), James Buchanan Brady Foundation, New York Hospital, Cornell University and the Department of Urology, Memorial Hospital, New York, N. Y.

A study was made of the pathology and prognosis of renal tumors encountered at the New York Hospital from 1932 through 1949, and at the Memorial Hospital from 1926 through 1949.

All clinical records bearing the diagnosis of "renal tumor" were surveyed. Of the 706 cases so designated, 411 cases were rejected because the diagnosis was based upon clinical findings unsupported by sound pathologic confirmation, or because the pathologic sections were unavailable. Thus, the study was limited to 295 cases in which adequate pathologic material was at our disposal. In each case the microscopic sections as well as the clinical record were reviewed and, in most instances, follow-up data were obtained.

The classification of renal tumors is the same as that employed by the authors in previous articles. This classification (table 1) is based on histopathology and histogenesis, and has prognostic value.

Renal celled tumors are designated as such because of their resemblance to the normal cells of the parenchyma. Grawitz[1] in 1884 considered them to be derived from misplaced suprarenal tissue. Stoerk[2] believed that they were nephrogenic and represented histologic variants of renal tissue. Later Ewing,[3] noting the prevalence of clear cells in these growths, called them "clear-celled carcinomas." In such tumors there is often a mixture of clear and granular cells arranged in solid cords, as tubules, or as papillae. Since these minor variations may exist in different parts of the same tumor[4] and since the exact provenance of the "type cell" is still a matter of speculation, subtypes have been omitted as superfluous. Also subclassifications of a descriptive sort have been omitted as unnecessarily cumbersome, even though they may have some prognostic significance. All these have been included under the term "renal celled carcinoma".

Transitional celled tumors of the kidney possess the architecture of transitional epithelium which lines the conducting portion of the urinary tract. They are comparable in architecture and behavior to similar tumors in the bladder and and may be nonmalignant papillary growths (papillomas) or transitional carcinomas. Through a process of metaplasia that does not necessarily lead to malignant change, they may assume epidermoid features.

Embryonal renal tumors, judged by their histologic resemblance to mesonephric tissue, may originate from a more primitive type cell which might be

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Read at annual meeting, American Urological Association, Washington, D. C., May 30, 1950.

[1] Grawitz, P.: Die Enstehung von Nierentumoren aus Nebennierengewebe. Arch. f. klin. Chir., **30:** 824, 1884.

[2] Stoerk, Oskar: Zur Histogenese der Grawitz'schen Nierengeschwulste. Beitr. z. path. Anat. u. z. allg. Path., **43:** 393, 1908.

[3] Ewing, J.: Neoplastic Diseases. Philadelphia and London: W. B. Saunders Co . 4th ed.

[4] Foot, N. C. and Humphreys, G. A.: The importance of accurate pathologic classification in the prognosis of renal tumors. Surgery, **23:** 369, 1948.

a rest, or a reversion of an adult form toward an immature cell. The composition of these tumors runs the gamut from a predominantly epithelial to a largely mesenchymal neoplasm. In the latter there are variable amounts of connective-tissue and muscle, well exemplified in the Wilms tumor. Cohnheim's theory of embryonal rests can explain the presence of such primitive cells within the renal parenchyma, whether they are suprarenal ("true hypernephroma") or multipotential mesenchymal cells. However, regression of adult cells to a more embryonal type is also an explanation. Studies of renal tumors[5] produced in male hamsters following the administration of stilbesterol suggest such a possibility.

TABLE 1. *Classification of renal tumors*

	TYPE	BENIGN	MALIGNANT
I. Derived from epithelium of renal parenchyma	Renal celled	Adenoma	Carcinoma
II. Derived from epithelium of conducting apparatus	Transitional	Papilloma	Carcinoma
III. Derived from rests or atavistic parenchymal cells	Embryonal		Carcinoma or carcinosarcoma a. Chiefly epithelial b. Mixed with mesenchymal elements (Wilms' tumor)
IV. Derived from supportive tissue	Connective tissue, fat, muscle, nerve, vessels	Fibroma Lipoma Myoma Neurilemoma Angioma	Fibrosarcoma Liposarcoma Myosarcoma Malignant nervous tumors Angiosarcoma
V. Derived from extrinsic sources by invasion or metastasis			Sympathoblastoma Pheochromoblastoma Metastatic carcinoma

Among the miscellaneous tumors arising in the supportive tissue of the kidney the pathologic type varies with the specific tissue of origin: connective-tissue produces fibromas and fibrosarcomas; fat, lipomas and liposarcomas; muscle, rhabdo- or leiomyomas and sarcomas; nervous tissue, neurilemomas or sympathoblastomas; and so on. Angiomas naturally arise in vessels. Extrinsic malignant tumors may metastasize to the kidney or invade it by direct extension from adjacent areas.

The incidence of the types of renal tumors encountered is set forth in table 2. The benign and malignant renal celled tumors were the commonest and malig-

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[5] Kirkman, H. and Bacon, R. L., Malignant renal tumors in male hamsters (Cricetus Auratus) treated with estrogen. Cancer Research, **10:** 122, 1950.

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The incidence of the types of renal tumors encountered is set forth in table 2. The benign and malignant renal celled tumors were the commonest and malignant transitional and embryonal tumors were next in frequency. While there were some nonmalignant transitional celled neoplasms, all the embryonal tumors were malignant. The incidence of growths of the supporting tissue was relatively low, as was that of tumors metastasizing to or invading the kidney.

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[5] Kirkman, H. and Bacon, R. L.: Malignant renal tumors in male hamsters (Cricetus Auratus) treated with estrogen. Cancer Research, 10: 122, 1950.

Adenomas were diagnosed clinically in 5 of 11 kidneys in which they were found. In the remaining 6 cases, the adenomas encountered were incidental to other lesions.* Neurogenous neoplasms probably invaded the organ from the suprarenal, but manifested themselves clinically as renal tumors. The metastatic testicular tumor was, in like manner, mistaken for a primary renal growth on the basis of pyelographic abnormalities.

A study of the survival rate of all patients operated upon before 1945 was undertaken. The results are tabulated by type of tumor in terms of 5 year and 10 year determinate survival after nephrectomy.

TABLE 2 *Incidence of renal tumors by pathologic types*

TYPE		BENIGN	MALIGNANT
Renal celled		11	167
Transitional celled		10	43
Embryonal	Epithelial		16
	Mixed (Wilms)		31
Supportive Tissue		3	9
Extrinsic			5
Total		24	271

One hundred and four patients with renal celled carcinoma were subjected to nephrectomy before 1945; 19 of these cases were indeterminate. Of the 85 determinate cases of renal celled carcinoma, 33 patients (38 per cent) were alive 5 years after nephrectomy. Four patients with proven metastases before operation are included in this series, but none survived more than 3 years. Fifty patients with renal celled carcinoma were subjected to nephrectomy before 1940; 10 of these cases were indeterminate.† Of the 40 determinate cases of renal celled carcinoma, only 9 patients (22 per cent) were alive 10 years after nephrectomy (fig. 1). A few patients who developed metastases postoperatively survived for many months. One showed metastases both to the skin and the skeleton for 3 years prior to death. Some of these patients received palliative x-ray therapy, but the evaluation of palliative measures is outside of the scope of this paper. Survival beyond the fifth year does not infer a cure of the disease. These tumors, by virtue of their leisurely rate of growth often require a 10 year observation for a definitive evaluation of prognosis.

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* These cases were included because a clinical diagnosis of "renal tumor" was made on the basis of pyelographic deformity At nephrectomy the abnormalities were found not due to tumor but incidental adenomas were encountered

† Indeterminate group classed as (1) Applied after treatment elsewhere, no evidence of cancer on admission or thereafter (2) Consultation only, no treatment requested (3) Patient refused proffered treatment or palliation (4) Dead within 5 years of other causes without recurrence of cancer (5) Lost track of within 5 years without recurrence of cancer

Twenty-one patients were subjected to nephrectomy prior to 1945 for transitional celled carcinoma; 2 of these cases were indeterminate. Of the 19 deter-

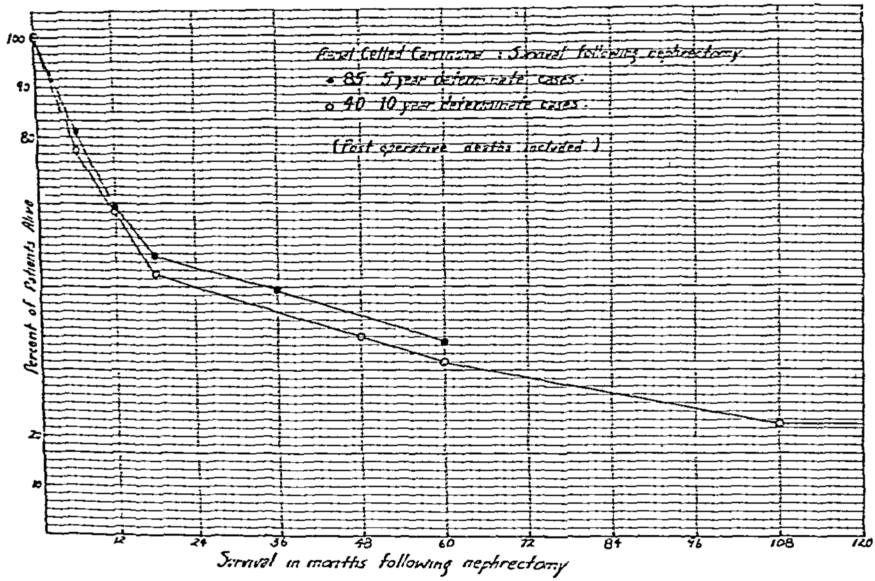

FIG. 1

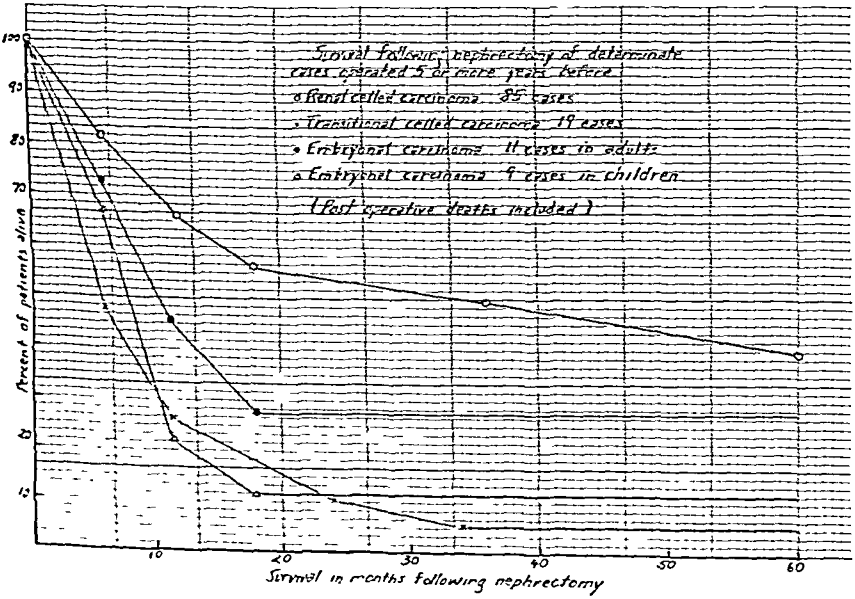

FIG. 2

minate cases, one patient was alive 5 years after nephrectomy (fig. 2). This patient died of cancer in the seventh year. There were also 7 cases of nonmalignant or simple papilloma according to our pathologic review. All patients survived 5-years after nephrectomy. Twenty-two patients were subjected to nephrectomy before 1945 for embryonal carcinoma of the kidney; 2 of these cases were indeterminate. Of the 20 determinate cases, 9 occurred in children and 11 in adults. Of the 9 determinate cases in children 1 patient (11 per cent) was alive 5 years after nephrectomy; this poor survival rate indicates the malignancy of this type. Of the 11 determinate cases in adults, 3 patients (27 per cent) were alive 5 years after nephrectomy.

The survival of patients with miscellaneous tumors of supportive tissue parallels the expectancy in the case of similar growths elsewhere in the body. Of the 7 determinate cases having various types of sarcoma, only 1 patient survived 5 years after operation. That patient is alive 17 years after nephrectomy for a leiomyosarcoma incidentally encountered in a tuberculous kidney. Of the patients with nonmalignant tumors one with a perirenal lipoma and one with a neurilemoma still survive.

The 5 year survival rate confirms the belief that nephrectomy is the operation of election as soon as the diagnosis can be established in any case of renal tumor. In the largest group, the renal celled tumors, the 38 per cent 5-year survival and the 22 per cent 10-year survival are gratifying. A tabulation of the 10-year survival is presented solely as a matter of interest, but not for definitive evaluation (table 3).

Although classification of these tumors according to type automatically indicates a prognosis to some extent, we sought to determine this still more accurately by analyzing the various types. In the case of malignant transitional celled and embryonal tumors the series were too small to justify conclusions determined through follow-up investigation. Until more adequate material becomes available, the separation of transitional papillomas from transitional carcinomas is all that we can establish with certainty: the latter have a poor prognosis. Similarly, in the embryonal group those predominantly epithelial bear a better prognosis than do those predominantly mesenchymal.

To determine the prognosis in the group of renal celled carcinomas, variations in the histopathology were further analyzed. Nineteen years ago, Hand and Broders[6] graded parenchymal renal tumors under four categories and reported their results. They demonstrated the prognostic value of grading, and this formalized previously held conceptions correlating the type of tumor and the prognosis, as well as establishing concrete histologic boundaries that might parallel a good or bad outlook. Similar work has been reported by us[7] in more recent years. Our analysis of histologic factors from previous experience has generally confirmed the soundness of such prognostication.

To summarize these factors: Those renal celled tumors with clear regular cells having isometric nuclei, arranged in cords and strands with *thick dense*

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[6] Hand, J. R. and Broders, A. C.: Carcinoma of kidney: Degree of malignancy in relation to factors bearing on prognosis. J. Urol., **28**: 199, 1932.

[7] Foot, N. C., Humphreys, G. A. and Whitmore, W. F.: The importance of accurate pathologic classification in the prognosis of renal tumors: Second report. J. Urol., **61**: 477, 1949.

TABLE 3. *Fate of 10-year determinate survivors*

	T	H	L	O	K	P	R	K	M
Symptoms	4 days hematuria, 3 yrs. frequency	3 years hematuria	6 months hematuria	3 weeks hematuria	Mass 5 years	3 mos. hematuria & pain in groin	1 year rt. flank pain	Rt. flank pain. 4 wks. hematuria	5 months gas
Exam.	Mass, pyel. defect	Mass, pyel. defect	Mass, pyel. defect	Mass, pyel. defect	Mass, pyel. defect	Pyel. defect	Tender kidney, pyel. defect	Pyel. defect	Mass
Sex, Age	55 F	17 F	63 M	53 M	11 M	10 M	51 F	57 F	15 M
Economic	Ward	Ward	Private	Ward	Private	Private	Private	Ward	Private
Path.	Tubular with septa	Tubular & solid	Irreg. cords. Septa with degeneration	Septa with islands	Papillary with septa	Solid and diffuse	Tub. & pap. with cysts. Encapsulated	Septa & acini, heavy cords	Cyst with small tumor invading wall
Size & Side	15 x 12 cm. Lower ½ L.	10 x 10 x 8 cm. Lower ½ Rt.	17 x 10 cm. Rt.	5 x 7 cm. Lower ½ Rt.	12 x 8 x 7 cm. Rt.	7 cm. Upper ½ Rt.	4 x 4 x 3 cm. Upper ½ Rt.	8 x 7 x 4 cm. Lower ½ Rt.	10 cm. cyst watery fluid over normal kidney.
X-Ray	Radiation terminally	None	Preop. radiation	None	Inadequate preop. rad	None	None	None	None
Metastases	9 yr. skin & flank, ilium	None	None	None	None	None	None	None	None
End-results	11 yrs. of ca. Died	13 yrs. L & W	11 yrs. L & W	11 yrs. L & W	10 coronary Died	10 yrs. L & W	10 yrs. L & W	13 yrs. L & W	17 yrs. L & W

Note: None of the above had demonstrable metastases, invasion of the renal pedicle, or perirenal tissues at time of operation.

septa offered the best prognosis; while those with irregular granular cells having anisometric nuclei arranged in tubules and papillae with irregular thin septa offered the poorest prognosis. Hemorrhage and cystic degeneration were considered favorable factors of secondary importance. On the basis of these histologic factors, the microscopic sections of 73 five year determinate cases were reviewed.

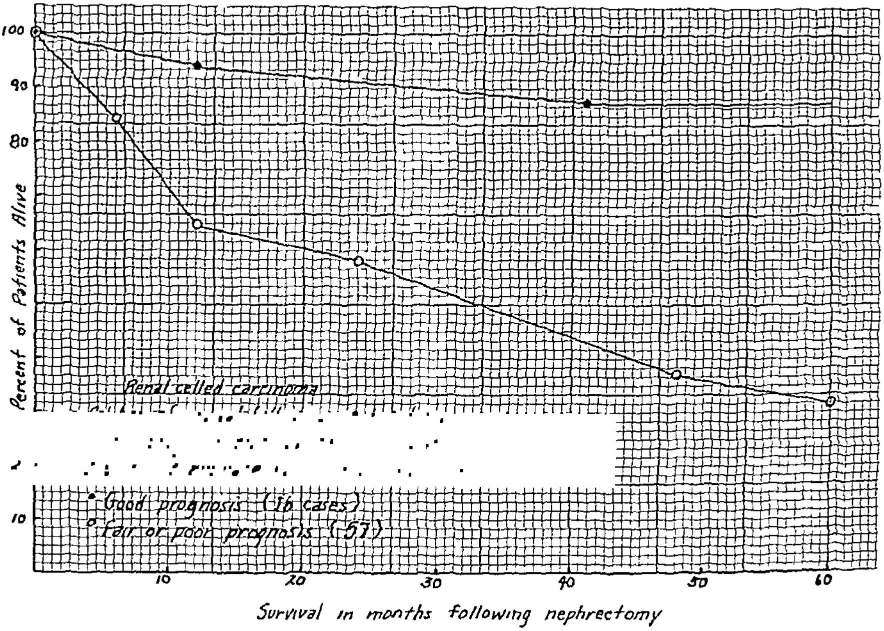

FIG. 3

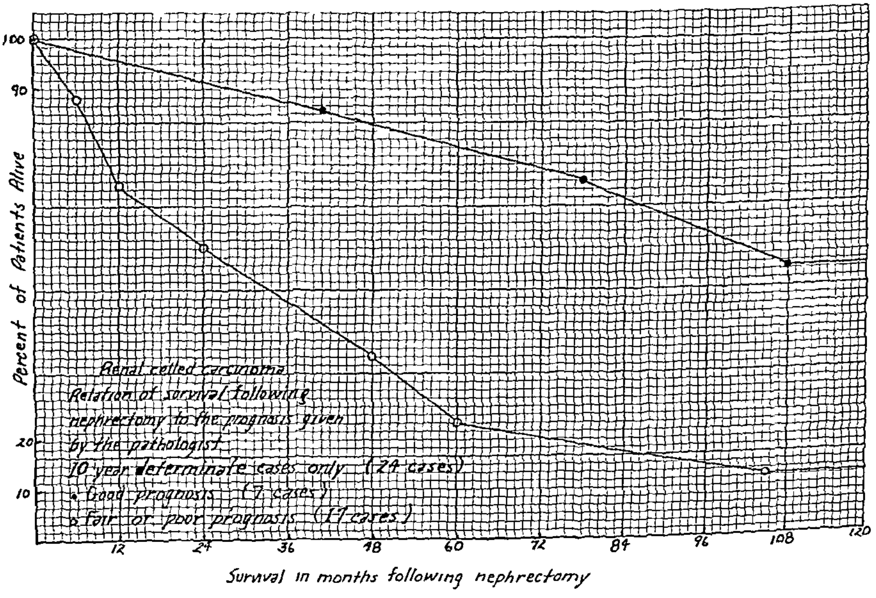

FIG. 4

We also divided the 10 year survivals into groups indicating poor and good prognosis. The results are graphically presented in figures 3 and 4. The method proved to be relatively accurate in prognosticating the outcome in the 5 year and 10 year groups. Initially we attempted to subdivide the poor prognoses into poor and fair prognoses. However, our estimated poor and fair prognoses were abandoned because they did not coincide with survival experience. Also from the table of 10 year determinate survivors, 7 of the 9 had what we called a "good prognosis," which seems to be the only factor in common amongst them.

SUMMARY

A pathologic classification of renal neoplasm is reviewed and restated. This appears to be practical and to be significantly correlated with prognosis. Survival rates according to the types of tumor are presented. Methods of evaluation of prognosis according to pathologic types of the tumors are discussed.

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DISCUSSION

DR. THEODORE R. FETTER (Philadelphia, Pa.): A study of this kind deserves considerable merit and consideration. One of the difficulties in the past in regard to renal tumors was the multiplicity of classifications. The various pathological classifications led to confusion. The authors have attempted to present a relatively simple and practicable classification which may be readily accepted. It is known that many variations may exist in different parts of the same tumor. Considerable experience in histopathology is necessary before one may even attempt to grade renal tumors in order to indicate a good or bad prognosis. Thus, if we are presented with a simple, precise and fundamentally sound pathological classification of renal tumors and an analysis of their histologic structure, we may infer that grading of these tumors will indicate the value of fairly accurate prognostication.

It is now appreciated that renal celled carcinomas with clear regular cells having isometric nuclei, arranged in cords and strands with thick dense septa offer the best prognosis; while, conversely, those with irregular granular cells having anisometric nuclei arranged in tubules and papillae with irregular thin septa offer the poorest prognosis. Cystic degeneration and hemorrhage are favorable factors but of secondary importance. There may be isolated exceptions to these conclusions but, in a general sense, they are acceptable in practice.

From the clinical and surgical standpoint, it is a fact that if a renal celled tumor is properly removed, and there were no demonstrable metastases, no invasion of the renal pedicle or perirenal tissues, one may expect a reasonable survival period. There is every reason to believe that a good prognosis may be given to the patient. On the other hand, the present day thinking in cancer is that even if the above conditions exist, the patient may eventually die of metastases. The findings of the authors more or less corroborate this thought. One must not become discouraged because the pathological evidence does not appear to compare favorably with our operative findings or clinical interpretations. The 5-year survival rate should convince us that nephrectomy is the operation of election as soon as the diagnosis of renal tumor is established. In the majority of clinics the 5-year survival rate varies between 30 and 40 per cent.

It will be interesting to note whether or not the 5-year survival rate will improve with the more widespread employment of the newer cytological methods of diagnosis. Recent reports appear to indicate that it is possible to make a fairly accurate diagnosis of renal tumor before the tumor attains reasonable size and/or causes a deformity of the calyceal architecture. This thinking is in line with our teaching that the early diagnosis of cancer and subsequent removal of the tumor will improve our survival period proportionately. It is well to interpolate at this point that many so-called essential hematurias may be due to renal tumors. It is a rule in our clinic that unexplained hematuria after the usual diagnostic procedures have been accomplished and failed to establish a diagnosis, repeated cytological studies of the urine must be done. We have not uncovered any renal tumors thus far, but in a recent personal communication I was informed that a diagnosis of probable renal tumor was made by cytologic study and at operation a small renal celled carcinoma was found.

In a study of renal tumors, it is noted that frequently patients survive a 5-year period or even a 10-year period and die of other causes without recurrence of cancer. One may well inquire whether or not the patient was cured of cancer. This is difficult to answer as far as present survival experience is concerned. Certainly more concrete evidence is necessary before any positive statement can be made. If one has such information in isolated cases the data should be reported to the tumor registry of our Association. It is obvious that the report must include a postmortem examination for proper evaluation in survival determinate series.

Prognosis of transitional cell tumors presents a different problem. Cytological study of the urine should offer a means to improve our survival period in this group. In the benign or malignant papillary types of transitional cell tumor the prognosis is more favorable than the flat or epidermoid transitional carcinoma. In the latter group the tendency to invasion of the pelvic wall and peripelvic tissues is well known. In general, the prognosis may be stated as very poor.

Certainly in the embryonal group one may expect a poor survival rate. Those tumors predominately epitheloid indicate a slightly better prognosis than those predominately mesenchymal such as the Wilms tumor in children.

It is interesting to note the pendulum swinging away from postoperative radiation in these tumors. Prophylactic radiation is no longer considered good therapy. If the tumor has been completely removed, there should be no need for radiation therapy. On the other hand, if metastases are present, there already is an existing handicap on the survival period with or without radiation therapy.

The presentation by these authors is a valuable contribution to the present knowledge of renal tumors and I wish to thank them for the privilege of discussion.

Slide 1 represents a patient, aged 21, female. Right nephrectomy 1942, renal cell carcinoma, living and well, subsequently married and mother of two children; no demonstrable metastases to date.

Slide 2 represents a patient, aged 37, female, right nephrectomy, in 1933, renal cell carcinoma, living and well, no demonstrable metastases. This is the longest survivor in our group.

Slide 3 represents a patient, aged 44, male, right nephrectomy in 1940. Died in 1946 of coronary occlusion. Postmorten revealed no cancer recurrence.

Slide 4 represents a patient, male, aged 36, left nephrectomy, doubtful normal left pyelogram, widening of the superior pole of the kidney; diagnosis, of suspected tumor, made in 1947, operated 1949, only symptom intercostal pain.

Slide 5 represents the specimen; renal cell carcinoma. Note the fairly thick margin of capsule surrounding the tumor.

DR. M. M. MELICOW (New York, N. Y.): I would like to congratulate Drs. Humphreys, Foot and Whitmore for their clear, concise presentation. Their classification is similar to the one we adopted at the Squier Urological Clinic.

I do think, however that their term 'renal-celled' carcinoma is an awkward one; we do not say 'stomach-celled' carcinoma for carcinoma of the stomach, why say 'renal-celled' carcinoma of kidney? We too have found that the clear cell carcinomas gave a better prognosis than did the other groups. We also found that metastases from a renal cancer may take a long time before showing up. In 2 cases, one 10 and another 14 years following nephrectomy (the latter in a female patient with vascular invasion by tumor cells which were found in the operative specimen); distant metastases grew imperceptibly for the intervals mentioned. The second patient presented a lung lesion which looked like a primary neoplasm, but proved to be a metastasis from a clear cell carcinoma of the kidney. The granular cell carcinomas gave a decidedly worse prognosis. One must emphasize, however, that there are some renal tumors in which both types of cells, clear and granular, are seen.

The mesodermal origin of renal tissue is demonstrated by the not infrequent 'sarcomatous' alteration in a clear or granular cell carcinoma; particularly upon breaking of barriers. The cells assume a spindle shape so that they are reported as true sarcomas or carcinosarcomas.

We found that the transitional cell, or preferably, the urothelial cell tumors, were either papillary or nonpapillary. The papillary tumors were often accompanied or followed by similar tumors in the ureteral, vesical or urethral tracts. The nonpapillary were often of the squamous cell type and gave a poor prognosis. Their presence was not recognized for a long time. The patient came with a hydronephrosis, or with a calculus shadow, or with a cryptic fever, or with a pronounced leukocytosis. Unless excretory urograms were made or tumor cell studies instituted the cases were missed. It is in these types of renal tumors, those of the pelvis, that tumor cell studies offer a chance for early detection. The clear and granular cell carcinomas, unless they have broken through into the pelvis, are not apt to reveal themselves through urine cell studies.

DR. GUSTAVUS A. HUMPHREYS (New York, N. Y.): I would like to thank the discussers, both Dr. Fetter and Dr. Melicow, for their kind and informative discussion on this subject. As pointed out, particularly by Dr. Fetter, the problem of early diagnosis is a great factor in being able to offer the patient an operation which might be calculated to give him a cure rather than palliation, if such can be obtained. In that respect, exfoliative cytology may be helpful.

I think the proper use and evaluation of the Papanicolaou technique is a very important diagnostic aid in kidney tumors but I do not believe that we could preclude the possibility, of course, of the presence of a renal tumor or necessarily feel too free in making that diagnosis unless we did have some confirmatory pyelographic change. In one case at New York Hospital, we were able to pick up renal carcinoma *in situ* and we trust that nephrectomy will give us the desired cure.

I would like to thank the discussors for their kind acceptance of our classification. I would like to suggest that its more broad use, possibly even by the Tumor Registry, might help us all clarify the kidney tumor problem by simplifying it, as well as giving us some idea of prognosis.

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SURGICAL MANAGEMENT OF BLADDER STONE

FRANCIS PATTON TWINEM AND BENJAMIN BRUCE LANGDON

From the James Buchanan Brady Foundation for Urology, New York Hospital, New York, N. Y.

In all the annals of medical history there is no more fascinating chapter than the surgical treatment of vesical calculus. In 1727 James Douglas wrote, "Stone in the bladder is a Distemper, which, for ought we know to the contrary, is as ancient as any other to which the humane Body has ever been subject." Among the Egyptians and Hindus, cutting for stone was performed many centuries before Christ. The Hippocratic Oath states, "I will not use the knife either on sufferers from stone, but I will give place to such as are craftsmen therein."

The first well recognized operation for bladder stone was "le petit appareil," a perineal lithotomy popularized by Ammonius of Alexandria in the third century B.C., and requiring only a knife and a hook. This operation remained essentially unchanged until about 1520 A.D., when Joannis de Romanis of Cremona devised a better perineal operation which was described 15 years later by his pupil Marianus Sanctus and thus became known as the Marian operation, or "le grand appareil," so called because of the more numerous instruments required for its performance. In this operation a grooved sound was first passed and the bulbous urethra opened with a lithotome. A gorget was then passed along the groove to steer the forceps into the vesical neck. The stone was seized with either straight or curved forceps and extracted. If this failed, a dilator was passed and the vesical neck divulsed sufficiently to permit extraction of the stone. The mortality of this procedure was high and rectal injury was frequent.

The next modification was the use of lateral lithotomy in which the incision was made just mesial to the left ischium. The originator and chief exponent of this operation was Frère Jacques, a former French trooper who flourished in the latter part of the seventeenth century and attained a wide reputation as an itinerant lithotomist. He concerned himself but little with postoperative care, stating, "I have extracted the stone; I leave God to cure the patient." Later, Cheselden was the most skillful lateral lithotomist, and 200 years ago, operated upon 213 patients with a mortality of 9.3 per cent.

Franco, in 1556, was the first to employ suprapubic lithotomy, but this operation was used but little until the latter part of the last century. Its more general use was retarded by the development of lithotripsy which appeared to be a great advance over a cutting operation without anesthesia.

Crushing calculi by open operation was probably known to Ammonius about 230 B.C. Sanctorius, in 1626, devised a crude instrument for crushing stones without opening the bladder, but it was not until the time of Civiale, in the early nineteenth century, that the operation could be performed with reasonable efficiency and safety. Civiale was involved in many arguments as to priority

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Read at annual meeting, American Urological Association, Washington, D. C., May 30, 1950.

with Leroy d'Étoilles and Heurteloup. Civiale's instrument consisted of two metal tubes, the inner tube having three curved projections by which the stone was grasped and held while a sharp iron rod was used to bore a hole in it. Several treatments were required to pulverize the stone. Weiss invented a curved screw lithotrite in 1824 and Heurteloup designed his curved percussion lithotrite in 1833. It was Bigelow, a Bostonian, who perfected the lithotrite, and in 1878 employed the modern operation of litholapaxy in which the calculus is crushed and the fragments evacuated through a metal tube at the same sitting. Since Bigelow's time little change has occurred in the procedure of litholapaxy except the introduction of the visualizing lithotrite which is preferred by some operators.

TABLE 1. *Replies of 210 urologists to questionnaire*

Visualizing lithotrite preferred	128
Nonvisualizing lithotrite preferred	64
Employ both, no special preference	16
Never employ litholapaxy	2
Of those using visualizing lithotrites:	
Prefer Ravich type	73
Prefer Hendrickson type	68
No preference	14
Few use other types Lowsley, Young, Wolf, Kirwin	
Never use a visualizing lithotrite	14

TABLE 2. *Accidents during litholapaxy*
(Compiled from questionnaire replies)

Total accidents	67
Breakage of lithotrite	37
Jamming of jaws of lithotrite	18
Bending of lithotrite	7
Rupture of bladder	4
Separation of parts of instruments with cystotomy	1
Accidents requiring cystotomy	27
Marked urethral trauma; cystotomy not required	

To determine the point of view of urologists throughout the country in the treatment of patients with vesical calculus, a questionnaire was sent out and 210 replies were received (table 1).

Although a visualizing type of lithotrite was preferred by 128 urologists, a preference for the nonvisualizing type was expressed by 64. It was noted that the majority of the older urologists preferred a nonvisualizing type. The difference in point of view of various urologists was quite marked. One urologist stated that since we had visualizing lithotrites he considered it akin to malpractice to use a nonvisualizing instrument. Whereas, another urologist said: "Visualizing lithotrites, Phooey!" A third urologist asked why one should use a lithotrite at all when it is so simple to do an open operation.

Table 2 shows the various types of accidents reported by those answering the questionnaire.

Fourteen years ago, one of us (F. P. T.) became interested in determining the breaking strength of various types of lithotrites. The Engineering Department of Columbia University was consulted and 5 lithotrites were subjected to increasing force in a manner simulating the conditions of lithotripsy. The exact amount of pressure in pounds required to break each lithotrite was carefully determined. Recently, 4 more lithotrites of different types were similarly tested at Columbia University. The results of these tests are given in table 3.

TABLE 3. *Breaking strength of lithotrites*
(Tests made at Columbia University Laboratory)

I Light-visualizing, foreign make, 22F
Movable jaw bent at 140 lbs., broke at 153 lbs.

II Ravich, 19½F
Movable jaw bent at 450 lbs., broke at 490 lbs.

III Ravich, same as II but shoulder of movable jaw thicker.
Movable jaw bent at 500 lbs., broke at 550 lbs.

IV Ravich, 22F
Movable jaw bent at 650 lbs., broke at 712 lbs.

V Ravich 27F
Movable jaw broke at 637 lbs.

VI Alcock 27F
Bend in tubing at 450 lbs., shaft broke at 476 lbs.

VII Hendrickson, 27F
Shaft broke at 962 lbs. (5 cm. from distal end)

VIII Bigelow type, 18F
Movable jaw bent at 650 lbs., broke at 762 lbs.

IX Bigelow, 24F
Movable jaw bent and broke at shoulder at 315 lbs.

TABLE 4. *Amount of force applied manually by a man of average strength*

Ravich	One hand	60–70 lbs.
	Two hands	110 lbs.
Alcock		160 lbs.
Bigelow, large wheel		300 lbs.

Table 4 shows amount of force that can be applied manually to the jaws of the lithotrite by a man of average strength.

It is seen from table 4 that if one uses a strong type of lithotrite and the lithotrite is in excellent condition, a man of average strength or even considerably greater than average strength cannot exert enough force manually to break the instrument. One lightly constructed visualizing instrument of foreign make was broken at 153 pounds' pressure. Such an instrument would be unsafe to use.

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The numerous accidents reported in table 2 with 37 instances of lithotrite breakage indicate that many of these instruments must not have been in excellent condition or such breakage should not have occurred.

Some bladder calculi have been measured, the amount of force required to crush them determined, and the fragments then chemically analyzed. Table 5 gives the result of these tests.

The force required to crush these stones was measured under conditions approximating as closely as possible those prevailing during lithotripsy.

It is seen from table 5 that the amount of force required to crush some calculi is greater than the breaking strength of a light lithotrite. From the size of the calculi listed, it can be concluded that there are undoubtedly some large, hard calculi which would require a force exceeding 400 pounds to crush.

TABLE 5. *Force required to crush bladder calculi*

COMPOSITION	DIAMETER (CM.)	FORCE (LBS)
Calcium oxalate	2.0	49.0
Calcium oxalate and calcium phosphate	1.1	62.0
Calcium oxalate and calcium phosphate	2.2	150.0
Uric acid	1.6	52.0
Uric acid	1.5	58.0
Uric acid	1.8	142.0
Phosphatic	1 1	18.0
Phosphatic	0.6	20.0
Phosphatic	0.8	22.8
Phosphatic	1.0	26.0
Phosphatic	1.3	35.0
Phosphatic	1.3	45.0
Phosphatic	1.1	81.0
Phosphatic	2.9	208.0
Phosphatic	3.2	218.0

Some years ago, tests were made by one of us (F. P. T.) at the Columbia University Testing Laboratory to determine by using a series of artificially constructed spheres of cement and sand, how the required crushing force varies with the diameter of the artificial stone; whether this force varies directly as the diameter—as the square of the diameter—or otherwise. Table 6 shows the results of these tests.

The results indicate that for the materials employed compression strength varies approximately as the square of the diameter. However, the materials used in these experiments are somewhat harder than most bladder calculi and previous experiments indicated that for softer materials, the exponent could be nearer 1 than 2. It is therefore highly probable that the compression strength of bladder stones varies as the diameter raised to an exponent which may vary between 1 and 2 depending upon the composition and hardness of the stone. With very hard stones, compression strength probably varies approximately as the square of the diameter, whereas with softer stones, the variation would be more nearly a direct proportion.

A clinical study has been made of the cases of vesical calculus occurring at the New York Hospital during the years 1933–1950. Three hundred and sixty nine cases were thus studied in detail and the more important findings derived from this study are given in the following tables.

Of these 369 cases, 349 occurred in males and 20 in females, a ratio of 17.5 to 1.

Table 7 gives age distribution by decades and also the percentage of patients with bladder calculi less than 30 years of age at different periods at the New York Hospital.

TABLE 6. *Relation between diameter of stone and compressive strength*

	NUMBER OF TESTS	N (EXPONENT)
Quartz	27	2.06
Silica sand-cement	20	1.4
Phosphate rock-cement	27	2.13
Limestone natural	30	2.16
Sand-lime	30	2.10
Average		1.97 (or 2.00)

$W = Kd^n = Kd^2$. (W = compression strength—K = a constant—d = diamet.—n = exponent)

Example—A stone 1.4″ in diameter has crushing strength of 150 lbs. What force is required to crush a stone of same material 2″ in diameter?

$$\frac{W}{150} = \frac{K(2.0)^2}{K(1.4)^2};\ W = 306 \text{ lbs.}$$

TABLE 7. *Age distribution by decades*

1ST	2ND	3RD	4TH	5TH	6TH	7TH	8TH	9TH
3	2	7	13	36	82	138	79	9

Percentage of patients with bladder calculi less than 30 years of age at different periods at the New York Hospital

1820–1846	1846–1866	1866–1920	1920–1937	1933–1950
83.3%	71.4%	26.9%	10.9%	3.25%

Table 7 shows only 5 patients since 1933 under the age of 20 years. The decreasing incidence of bladder calculi in young people from 1820 to the present time is very striking. Whereas in 1820–1846 more than four fifths of the patients were less than 30 years of age, in this study only 3.25 per cent of the patients are in that age group. This finding has also been made in studies in England and elsewhere. The marked change in age grouping has undoubtedly been due to improvement in the diet of children.

In size, the calculi varied from those a little less than a centimeter in diameter to the giant calculus illustrated in figure 1. The essential data concerning this calculus are given in table 8.

The man who had this giant calculus was a private patient of one of us (F. P. T.), and who gave as his chief complaint "I have an ache in my prostate." The calculus was removed without difficulty and 3 weeks later a transurethral prostatic resection was performed. The patient made a very satisfactory recovery. After having dried out for a period of a week the weight of the calculus was 446 gm. Had the calculus been weighed immediately, the weight would certainly have exceeded 500 gm.

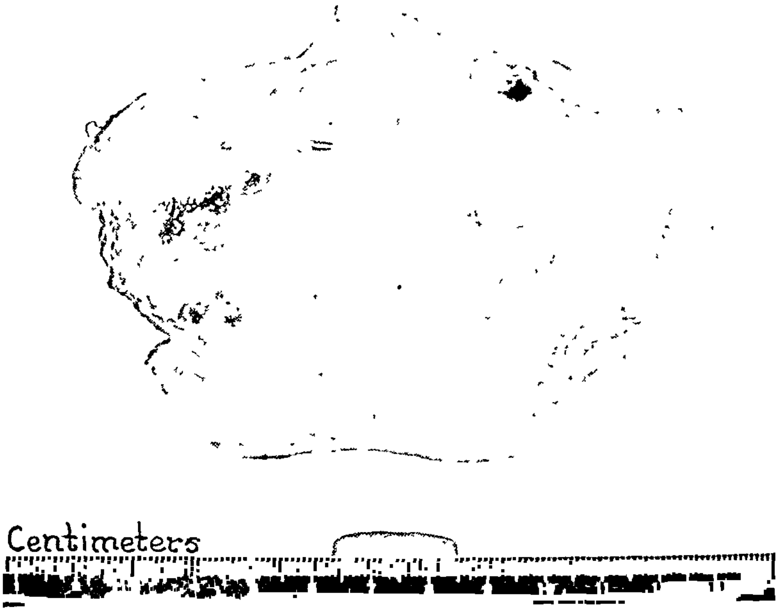

FIG. 1. Giant vesical calculus removed from 63 year old man whose only complaint was "ache in prostate." Three weeks later a transurethral resection was done, and patient made an excellent recovery.

TABLE 8 *Giant vesical calculus*

Circumference in two planes 32 cm. and 31.5 cm.
Diameter 12 cm. x 8.5 cm.

Weight (after a week of drying) 446 g.

Culture from interior of calculus
Streptococcus non-hemolyticus and Gram negative bacillus
Chemical composition
Triple phosphate with traces of urates and calcium oxalate.

Removal by cystotomy was followed 3 weeks later by transurethral prostatic resection. Patient did well postoperatively.

Table 9 shows the types of operations performed. Of these, 219 were open operations and 146 were closed. Of the open operations, 168 were simple cystolithotomies. In the other 51 cases, the removal of the calculi was associated with some other operative procedure.

TABLE 9. *Types of operations*

OPEN—219	CLOSED—146
Closed	
True litholapaxy (stone crushed and washed out)	104
Unsuccessfully attempted litholapaxies	17
Removal transurethrally without crushing, (rongeur, forceps or irrigation)	25
	146
Types of Open Operations	
1 Simple cystolithotomy	168
2 With one stage suprapubic prostatectomy	33
3 Perineal prostatectomy	12
4. With diverticulectomy	2
5 With transurethral prostatic resection	1
6 With segmental resection of bladder tumor	1
7 Retropubic prostatectomy	1
8 With suprapubic fulguration of bladder tumor	1
	219

TABLE 10. *Relevant associated conditions*

Obstructions to urinary outflow	312
Nephrolithiasis	56
Diverticula of bladder	35
Bladder tumors	22
Bladder fistulas	9
Neurological bladder	13
Foreign body in bladder	4
Radon ulcers	3
Cystoceles	2
Parathyroid tumor	1

TABLE 11 *Nonfatal complications of cystolithotomy*

Pulmonary emboli	3
Thrombophlebitis	2
Coronary infarction	1
Septic temperature	3
Wound reopened	3
Postoperative hemorrhage	3
Epididymitis	4
Lobar pneumonia	3
Anuria (for 3 days)	1

The various related conditions complicating cystolithiasis are shown in table 10 Of course, the most commonly associated condition was that of obstruction at the bladder neck, which was demonstrable in 312 cases (84 per cent). Stone

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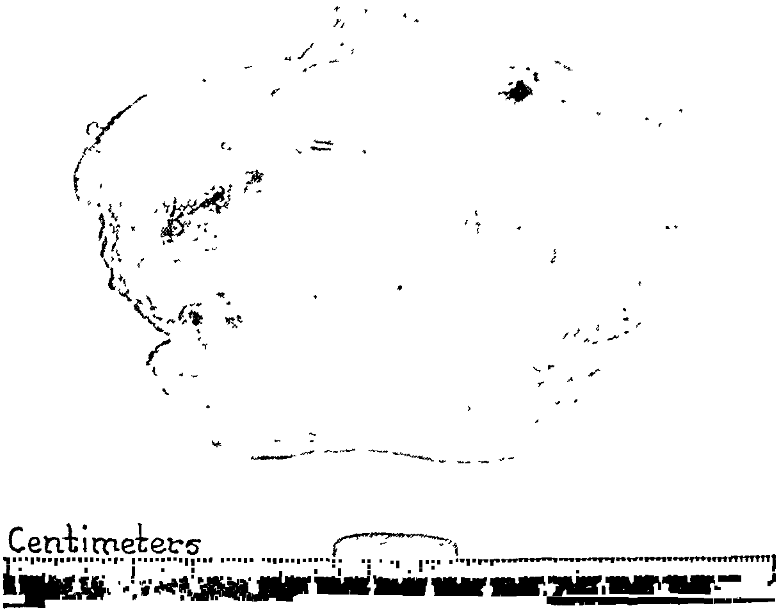

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The various related conditions complicating cystolithiasis are shown in table 10. Of course, the most commonly associated condition was that of obstruction at the bladder neck, which was demonstrable in 312 cases (84 per cent). Stone in the kidney occurred in 56 cases. There was only one case of demonstrable parathyroid tumor.

Table 11 shows the various nonfatal complications of the cystolithotomies

TABLE 12. *Complications of litholapaxy*

Perforated bladder	3
Perforated urethra	3
Traumatic bladder ulcer	2
Excessive bleeding during procedure (operation discontinued)	2
Postoperative hemorrhage	2
Marked postoperative sepsis (*in addition to those having the above traumatic injuries*)	2
Epididymitis . . .	1
Mortality of litholapaxy	1 (0 7%)
Cause of death, perivesical cellulitis and multiple abscesses (Staph aureus)	

TABLE 13. *Incomplete litholapaxies*

Poor anesthesia (bladder spasms)	1
Evacuation equipment not available	1
Hemorrhage	2
Lithotrite jammed	1
Impossible to introduce evacuator tube	1
Stone too hard to crush (Ravich badly bent)	1
No clear explanation, but procedure discontinued and cystolithotomy done	8
Completed by litholapaxy at later date	2
Total	17

TABLE 14. *Composition of calculi*

Phosphatic ($CaPO_4$, $CaCO_3$, $MgNH_4PO_4$)	138
Uric acid	55
Oxalate	35
Oxalate and phosphate	25
Phosphate and urate	12
Oxalate and urate	7
Oxalate, urate and phosphate	7
Cholesterol	1
Phosphate, urate, and sulfate	1
	281
No analysis	88
	369
Calculi with foreign body nucleus	4
Hair pin, 1; Gauze (absorbable), 1	
Prostatic tissue, 1; Silkworm gut, 1	

Table 12 shows the complications involved in 146 litholopaxies. These complications were not included in the complications listed previously in the discussion of the questionnaire results. It is seen that serious complications during litholapaxy are not uncommon. This is not surprising when one considers that most of the surgeons who do litholapaxies do them only occasionally. The surgeons in some parts of India who do many hundreds of these procedures and consequently become more skillful in this type of operation, have proportionally fewer accidents. The one death that occurred in this series of litholapaxies occurred as a result of perivesical cellulitis and multiple abscesses (Staph. aureus). Table 13 lists 17 litholopaxies which were not completed for the reasons specified.

Table 14 shows the composition of the removed calculi. As one would expect, phosphatic calculi were by far the most numerous. There were four calculi which had formed around a foreign body nucleus. The nature of the foreign body is stated in the table

Table 15 shows the frequency of various types of infecting organisms.

Table 16 lists the mortality in 219 cases of cystolithotomies including associated operations. The cause of death is given in the table. If one eliminates those cases in which some other major operation accompanied cystolithotomy, one arrives at the figure of 12 deaths in 168 cases of simple cystolithotomy (7.14 per cent).

TABLE 15. *Infecting organisms*

Nonhemolytic streptococcus	38
Staphylococcus albus	35
Bacillus proteus	29
Bacillus coli	27
Aerobacter aerogenes	25
Staphylococcus aureus	24
Pseudomonas pyocyaneus	20
Bacillus subtilis	5
Diphtheroid bacilli	5
Hemolytic streptococcus	5
No culture but over 15 WBC per HPF	136

TABLE 16. *Deaths: Cystolithotomy in* 219 *cases*, 21 (9.6%)

General sepsis with bacteremia	4
Postoperative hemorrhage (prostatectomy)	2
Thrombophlebitis and pulmonary emboli	6
Pneumonia	3
Acute pulmonary edema	1
Shock	1
Uremia	1
Sudden death (cause?)	1
Intestinal hemorrhage	1
Anesthetic death (spinal)	1

CONCLUSIONS AND COMMENT

Choice of the proper type of operation in cases of vesical calculi depends on the age and physical condition of the patient, the size and hardness of the stone, the presence or absence of urethral stricture, prostatic hypertrophy or other associated conditions, and the experience and skill of the operator. A greater degree of skill is required to perform litholapaxy properly than to do a suprapubic lithotomy. Litholapaxy has two advantages over open operation: 1) a shorter period of convalescence; 2) a lower mortality. In this series the mortality of litholapaxy was only 0.7 per cent, whereas the mortality of simple cystolithotomy was 7.14 per cent.

It is believed that the complications of litholapaxy can be greatly reduced by careful attention to the details of proper technique. Most urologists who do this procedure perform it only occasionally and consequently have a higher percentage of complications than they would with increased experience.

The exact amount of force necessary to crush calculi, varying in size and composition, has been determined.

The extreme limits of crushing strength of nine lithotrites were determined and are reported in this paper.

There are some lightly constructed lithotrites which are not sufficiently strong to crush very hard calculi of even moderately large size.

The stronger lithotrites have sufficient strength so that one cannot apply manually enough force to break the lithotrite. (This assumes that the lithotrite is in excellent condition.) In many of the reported accidents, the lithotrite could not have been in first class condition.

It has been established that the amount of pressure required to crush vesical calculi of *varying size and composition is proportional to the diameter* raised to an exponent which varies between 1.2 and 2, depending upon the hardness of the calculus.

In general, the visualizing lithotrite is suitable for smaller stones but the nonvisualizing instrument is more satisfactory for the larger ones. The use of a rongeur in handling a stone of any considerable degree of hardness is dangerous and many accidents have been reported from this cause.

A decreased incidence of bladder calculi in the young in recent years, as compared with a century ago, is very striking. This is believed to be due to the greatly improved diet of children.

A case of giant bladder stone (32 cm. by 31.5 cm.) is reported.

A clinical study of 369 cases of bladder calculi is reported.

The authors wish to express their appreciation of the very kind assistance given by Professors Krefeld and Ingalls of the Department of Engineering, Columbia University, New York City: We also wish to thank Mr. Frederick J. Wallace, president, American Cystoscope Makers, Inc. for his most helpful cooperation.

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REFERENCES

Barney, J. D.: History of Urology, American Urological Association. Baltimore: Williams and Wilkins, 1933, vol. 2, chapter 1.

Crance, A. M.: Removal of a giant vesical calculus with aid of obstetrical forceps. J. Urol., **45**: 327, 1941.

Cristol, D. S. and Greene, L. F.: Vesical calculi in women. Surg. Clin. North Am., **25**: 987, 1945.

Prentiss, R. J.: Vesical calculus: Clinical study based on 250 cystolithotripsies and 132 cystolithotomies. J. Urol., **47**: 664, 1942.

Riches, E. W.: Some landmarks in surgery of stone. Brit. J. Urol., **7**: 140, 1938.

Twinem, F. P.: One hundred years of bladder stone surgery at the New York Hospital. Urol. & Cutan. Rev., **42**: 313, 1938.

Twinem, F. P.: Surgical removal of vesical calculus: An experimental and clinical study. J. Urol., **41**: 360, 1939.

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DISCUSSION

Dr. Gershom J. Thompson (Rochester, Minn.). Doctors Twinem and Langdon have given an excellent historical review of the treatment of vesical calculus. One can well imagine the morbidity and mortality which followed procedures like lateral perineal lithotomy, or urethral and bladder neck divulsion for the extraction of large stones, especially when followed by inadequate drainage and with no attempt whatever being made toward the correction of the obstructive process which usually is responsible for stone formation. The statement "I have extracted the stone; I leave God to cure the patient" is indeed correct.

The contributions of many men toward the development of the art of litholapaxy is admirably discussed by the authors who themselves contribute much by their experiments designed to prove the strength of lithotrites. I was especially interested to learn that a man of average power cannot break a well constructed lithotrite which is in good condition; this confirms my own experience and is somewhat reassuring. On occasions the muffled dull clunk which usually climaxes great exertion on a well grasped stone has momentarily made me wonder which broke, the stone or the lithotrite; from now on I shall worry less. Given strong lithotrites it is up to us to care for them and use them properly. Thorough drying and oiling after use are important; merely flushing the debris off with water and throwing it back on the shelf is a poor way to treat an instrument. Inspection prior to its use, then careful instrumentation supporting the perineum by gentle finger pressure when the beak approaches the triangular ligament, and above all avoiding brutal force, will insure success.

Winsbury-White's textbook best describes the technique of litholapaxy. It should be read carefully by anyone striving for perfection. I prefer to have the patient in the cystoscopic position throughout the procedure and use a direct vision cystoscope and evacuating syringe instead of the nonvisualizing evacuating tube and Bigelow pump. With the cystoscope one can quickly observe the thoroughness of lithotrity and lose no time in crushing large fragments which remain. I have always preferred the nonvisualizing instrument which, if used properly, is absolutely safe. It is only when one gets careless that trouble ensues. Thorough inspection of the entire bladder cavity and of any diverticula present will insure complete removal of all fragments and sandy particles, but one should routinely make a plain roentgenogram of the bladder area before dismissal because in a small number of cases stones will recur and the patient is quick to believe that his new stone has formed on a nidus which was left behind.

The choice of procedure between suprapubic lithotomy and litholapaxy will always remain an individual one as will the choice of the type of instrument. Very large stones must be removed by incision and some smaller ones in which other complications such as urethral stricture, vesical contracture, severe sepsis or huge intravesical intrusion of the prostate gland exist are best managed in this manner. However, with care the large majority of stones can be removed by litholapaxy.

The change in trend of management is illustrated by comparing two series of cases observed at The Mayo Clinic. In the 25 years prior to 1932 in a series of 1014 cases, 75 per cent were treated by suprapubic lithotomy and 25 per cent had litholapaxy. But in the 10 years preceding January 1, 1950, of a series of 841 cases only 4.6 per cent had suprapubic lithotomy and 95.4 per cent were cared for by litholapaxy.

My associates and I believe that litholapaxy and removal of the obstructing tissue at the vesical neck under the same anesthetic are sound, safe procedures and we will continue this practice for the large majority of cases, and use suprapubic lithotomy in only a few.

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VESICAL EVIDENCE OF POSTEROLATERAL SPINAL CORD DISEASE

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Some eleven years ago it was noted that in certain instances of atonic neurogenic vesical dysfunction, there appeared at the vesical neck region of the cystograms a deformity which we saw repeatedly and termed a "straight line defect". This abnormality in a relatively normal appearing cystogram consisted of a sharply cut off portion of the vesical neck (fig. 1). In the past 3 years certain aspects of neurogenic vesical dysfunction have been our major project and though we have not concluded the study, this report constitutes an interval note. The first publication from this investigation was that of "Vesical Abnormalities Incident to Diabetes Mellitus" which was read at Buffalo in 1947.

During the investigation of the "straight line vesical defect" in cystograms it was noted that it was not consistently present in vesical atonia, but always in conjunction with posterolateral spinal cord disease. We observed the "straight line defect" of the vesical neck in all instances of proven posterolateral spinal cord disease that we have had the opportunity to study. This list includes the secondary cord changes of pernicous anemia and diabetes mellitus, tabes dorsalis, syringomyelia, senile arteriosclerosis of the spinal cord vessels, some examples of spina bifida occulta, post rabies vaccine myelitis and allergic myelitis. In at least two cases we have seen the changes without being able to establish the precise neurological entity though there was present neurological evidence of posterolateral cord changes.

Upon careful analysis of the patients demonstrating cystographic abnormality it was found that the defect was distinct only if the bladder was not fully distended. If the bladder contained a certain amount of the opaque medium the "straight line defect" was often only faintly visible, overshadowed apparently by the anterior and posterior contour of the bladder at the apex which suggested that the defect was not only occasioned by an abnormality of the vesical neck per se, but caused by some structure within the bladder near the apex.

In patients in which the "straight line defect" occurred, a distinctly elevated interureteric ridge was observed on cystoscopic examination. The other findings associated with this condition which we have reported previously were also noted. The ureteral orifices are approximated with a marked bowing of the interureteric ridge with a resultant diminution of the trigonal altitude. The vesical neck is reduced in caliber due to a thickening of the tissues and there appears a concavity of the posterior urethra between the verumontanum and vesical neck with an apparent shortening of the posterior urethra. It was found furthermore that the "straight line defect" appeared only in the presence of residual urine.

The bladder revealing the cystogram defect was studied cystometrically. As

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Read at annual meeting, Southeastern Section, American Urological Association, Gulfport, Miss., February 3, 1950.

expected it was found that in every instance the cystometrogram demonstrated a typical and marked atonic curve. The cystometrograms demonstrated repeatedly that the degree of elevation of the interureteric ridge was directly proportional to the amount of vesical atonia. In using a water cystometer connected by a fluid system to a tambour it was found that tracings on a smoked drum showed in patients with a "straight line vesical defect" that the vesical contractions were of low amplitude. These cystometric studies suggested that detrusor activity was greatly dampened and these observations substantiated those of Denny-Brown.

Denny-Brown postulated that the intravesical pressure was not the factor that induced loosening of the vesical sphincter during the mechanism of voiding. The relaxation of the vesical sphincter was found to be reciprocal with contraction of the bladder. The greater the amplitude of detrusor activity or contraction the more the internal sphincter relaxed and, conversely, the more the bladder relaxed, the more the sphincter contracted.

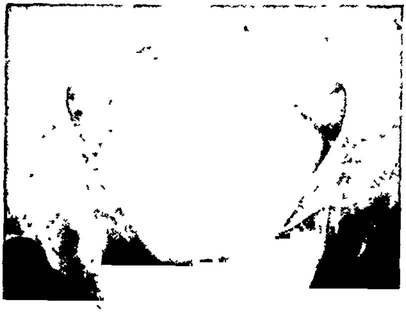

FIG. 1. Cystogram showing sharply cut off area of vesical neck ("straight line defect").

Our observations thus far in the problem do not present anything fundamentally new, but add only to the accumulated data in a well established literature. We were however unaware of previously reported consistent trigonal changes observed at cystoscopy and described fully as a part of posterolateral spinal cord disease. It was our aim to attempt to determine clinically whether or not the vesical neck or internal sphincter tonic state as described by Denny-Brown was a true mechanism of increased internal sphincter and trigonal tonus coupled with a lack of detrusor tone. In other words, are the vesical neck changes truly an active phenomenon or a passive phenomenon? With the interruption of the pelvic nerve impulses to the trigone and internal sphincter does this permit a static imbalance and allow the vesical neck to thicken and the detrusor to relax or is this an active process in which the impulses are constantly being discharged to the trigone for contraction and the impulses to the bladder absent or only partially effective? Or as the bladder becomes larger do the trigone and vesical neck become relatively smaller and more prominent and finally effect obstructive proportions? This problem of active vesical neck change as opposed to static variation was our next undertaking.

Animal experimentation was considered and discarded because of the inconstant vesical appearance even in the monkey. The measurement of trigonal and bladder muscle activity either independently or collectively was decided upon as the most logical means of investigation. An instrument comparable to the electrocardiogram was found unsuitable because of inconstant and uninterpretable results due to interference of uncontrollable striated muscle activity. At present we are studying an electronic method for measuring smooth muscle activity that is applicable to the bladder and can be used for differential studies of the trigone and detrusor. This work shows promise in determining quantitatively muscle activity by measuring smooth muscle electrical potential change in any portion of the bladder or urinary tract. This study will be reported in detail at a future date.

Recently we had the good fortune of seeing two patients in whom there was an acute posterolateral column lesion and we were able to study these patients cystoscopically soon after the onset of the pathological changes. In both patients it was found that the trigonal variation is apparently an immediate change. The degree was proportional to the amount of neurological involvement. These two cases will be reported to demonstrate our findings and their probable significance.

CASE REPORTS

Case 1. J. B., No. 84730 Norton Memorial Infirmary, a boy of 11 years, was referred by Drs. Spurling, Grantham and Segerberg because of urinary retention complicating a post rabies vaccine myelitis. Within a period of 2 weeks following the onset of myelitis, some of the patient's muscular activity returned, but he continued to have evidence of posterolateral spinal cord disease as evidenced by ataxia, loss of deep tendon reflexes and paresthesia.

An atonic bladder developed at the onset of symptoms, and the patient was observed cystoscopically on the ninth day of illness. At this time he demonstrated in the bladder a diminutive trigone, markedly elevated interureteric ridge, pronounced approximation of the ureteral openings and a perceptible recess in the posterior urethra located between the vesical neck and proximal portion of the verumontanum. Cystoscopically a typical picture of posterolateral spinal column disease was presented.

During the ensuing 8 weeks the patient's ataxia improved to a point of almost imperceptible presence, but the trigonal and posterior urethral changes persisted. Residual urine of 6 ounces continued without diminution. The tendon reflexes returned partially and subsequent improvement has been lacking.

A trigonal and vesical neck resection was considered imperative, but since the patient was a child, it was believed that the resection should be accomplished without urethral manipulation. The hypertrophied interureteric ridge and vesical neck were resected under direct vision using the retropubic approach (fig. 2). Convalescence was uneventful and the patient has been voiding without residual urine for several months.

Case 2. W. G., No. 84841 Norton Memorial Infirmary, a young robust male of 29 years, was referred to us by Dr. Lawrence T. Minish. Acute urinary retention developed some 27 hours after an antitetanus injection given as a prophylactic measure at the time of a superficial foot injury. The patient stated that at the age of 14 years he had a temporary paralysis of the lower extremities with urinary retention following a "serum injection" and was confined for a time to a wheel chair.

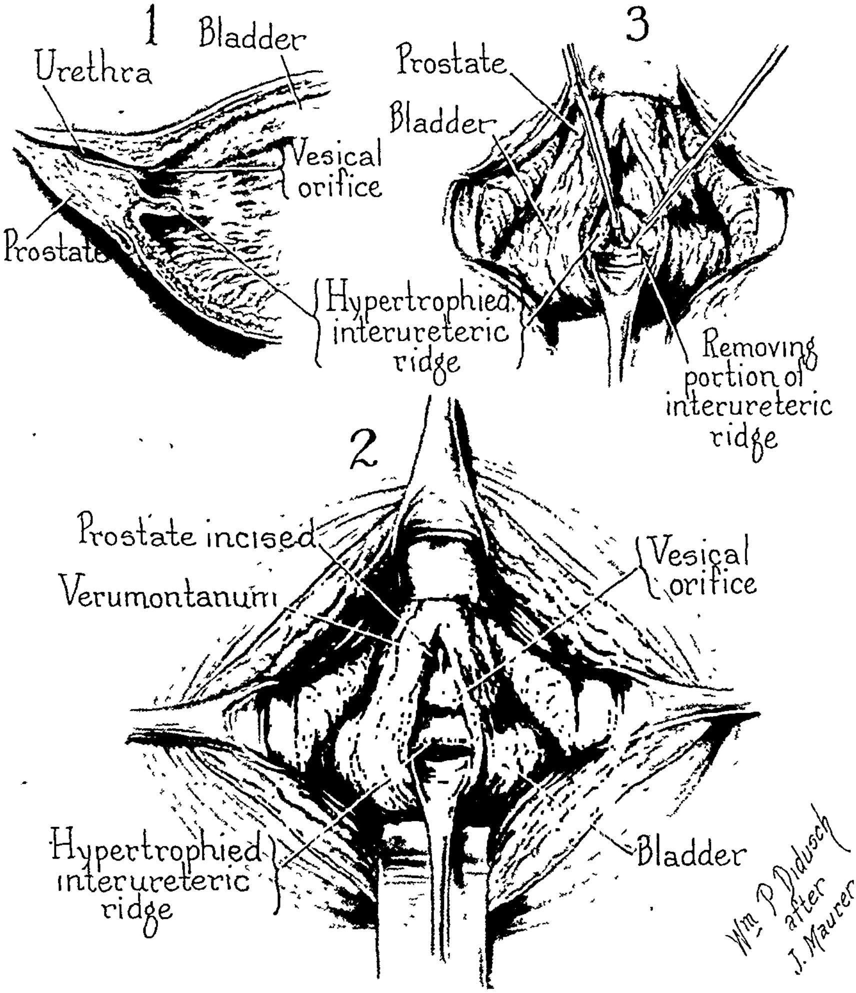
1
Bladder
Urethra
Vesical orifice
Prostate
Hypertrophied interureteric ridge
3
Prostate
Bladder
Removing portion of interureteric ridge
2
Prostate incised
Verumontanum
Vesical orifice
Hypertrophied interureteric ridge
Bladder
Wm. P. Didusch after J. Maurer

FIG. 2. Retropubic resection of interureteric ridge and hypertrophy of vesical neck.

The present illness was confined to an acute and peristent urinary retention and some unequal deep tendon reflex changes and paresthesia. Cystoscopically the patient presented the typical trigonal and vesical neck changes characteristic of posterior cord disease. The cystometrogram demonstrated a marked vesical atonia.

The patient was treated by an indwelling urethral catheter; after the catheter was removed he emptied his bladder with great difficulty by straining forcibly when the bladder was quite distended. Urination improved gradually and within a period of 3 weeks he was voiding normally. The abnormality of the vesical neck and trigone had disappeared and there was no residual urine. The neurological changes seen initially had vanished.

DISCUSSION

These patients represent our only opportunity to study cystoscopically the bladder within a short time after posterolateral spinal cord changes have become manifest. We have here in addition the unusual situation of an acute onset and a known etiological agent.

These observations suggest that the trigonal and vesical neck changes are an active phenomenon due to increased trigonal and sphincter activity. Their appearance was undoubtedly abrupt and complete. In the second patient (allergic myelitis) the entire vesical picture disappeared as the spinal cord lesion disappeared. In the first patient (post rabies vaccine myelitis) the obstructive vesical picture remained, as did many of the neurological changes.

An interesting observation is that of vesical trabeculation. In neither of the patients was trabeculation present initially and in the second patient it was never manifest. In the first patient it was observed first approximately 8 weeks after the onset of the vesical atonia. This relatively late appearance of vesical trabeculation would suggest that trabeculation is a purely secondary phenomenon dependent upon prolonged obstruction. It is actually muscle bundle hypertrophy and in bladder atonia the diminished but repeated vesical contractions are responsible for bladder trabeculation. The fine trabeculation of tabes dorsalis as compared to the massive trabeculation of prostatism is only a response to the ability of the bladder to contract.

CONCLUSION

A deformity of the cystogram is described in posterolateral spinal cord disease which is occasioned by an elevation of the interureteric ridge producing at the vesical neck a "straight line defect." Case reports of 2 patients are presented in which cystoscopic examinations were made soon after the pathological process occurred in the spinal cord. In both instances the trigonal and vesical neck changes suggested that the obstructive vesical neck changes were active muscular changes. The late appearance of trabeculation seemingly substantiates the contention that this is a secondary change dependent upon the degree of obstruction and potential activity of the detrusor.

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THE PRESENT UROLOGIC STATUS OF THE WAR-TIME PARAPLEGIC

JOHN A. HUTCH AND R. CARL BUNTS

Interest in the urological aspects of spinal cord injuries has increased greatly in the last few years. This is due to a number of factors: first, World War II, which unfortunately produced many such cases; second, the improved methods of treatment which have allowed large numbers of these patients to survive and third, to the establishment of centers for the care of these cases. Much of the literature concerning the paraplegic was written during and shortly after the war and described accurately the problems encountered during the first 12 to 24 months of the paraplegic condition. In this study, urological problems occurring in later stages of the paraplegic disease will be emphasized.

One hundred seventy cord injury patients have been analyzed in our report. They range in duration from 2 months to 22 years. Eighty-five (or 50 per cent) of the patients included received their injury during or before World War II. The entire group averages 4.04 years since injury.

Certain arbitrary definitions have been set up for convenience and will be applied throughout. The level of the lesion will include cervical, dorsal (D1 through D11) and lumbosacral D12 and below. The decision to include D12 as a lumbosacral lesion was determined because it is an intimate part of the conus medullaris. Housed within D12 and L1 vertebrae are the reflex centers for the bladder parasympathetics. The cord is so congested in this area that a lesion which would include the D12 roots and manifest itself on neurological examination as a D12 lesion could actually have injured the bladder reflex centers in the sacral cord. Therefore, a D12 lesion is classified as lumbosacral.

The basis of a large part of this study rests on the clinical classification of the bladder dysfunction into good and poor neurogenic bladders. A good neurogenic bladder refers to one which empties no more often than every 2 hours. It must be able to retain its contents without leakage for that period of time under conditions of normal exertion and normal fluid intake. The bladder must be able to empty to such an extent that the residual urine is under 100 cc. Complete nocturnal continence was not considered necessary to qualify a bladder as good since many of these patients have so little warning of a full bladder that it will not awaken them from sleep. A bladder which fails any one of these qualifications is considered a poor neurogenic bladder. There is also a third group which for one reason or another has never had a voiding trial. The 28 cases in this group are listed as "No Trial".

An arbitrary period of time has been established as the maximum duration of spinal shock. Sir John Thomson-Walker claims that spinal shock may last 18

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months and this period of time has been adopted in this paper. Therefore, any bladder which cannot empty its contents, but is less than 18 months since injury, is considered to be in spinal shock. Any bladder which cannot empty its contents and is more than 18 months since injury is considered a poor neurogenic bladder in the retention group.

THE LEVEL OF THE CORD LESION AND THE CLINICAL TYPE OF BLADDER WHICH HAS DEVELOPED

In attempting to correlate the level of the cord injury and its completeness with the clinical type of bladder which eventually developed (table 1), we were surprised to note that the poorest end results were in the thoracic group. We had assumed that it would be the lumbosacral group which developed the largest percentage of poor bladders. Excluding the "No Trial" cases we find that good neurogenic bladders developed in 63 per cent of the cervical lesions; in 37 per cent of the dorsal lesions and in 62 per cent of the lumbosacral lesions.

Some war time writers were very pessimistic about the outcome of complete lesions at or below L1. This is understandable since theoretically a lesion so placed could produce a complete severance of the bladder from its central nervous system connections. It is also stated by Martin and Davis that the closer the injury lies to the conus medullaris the greater is the time required for the bladder to develop automaticity. "Most patients with lesions of the conus medullaris or cauda equina require from 8 to 20 months, or longer, to develop automaticity." With this slow rate of recovery of bladder function, it is understandable that early observers placed such a grave prognosis on the lumbosacral lesions. Our own series shows that these lesions do as well or better than the higher cord injuries. There are a number of factors which work together to favor the patient with a low lesion. First, it is rare to have an injury so severe as to produce an autonomous bladder. (Of 57 patients with lumbosacral lesions tested by cystometric studies, 56 could generate an intravesical pressure of over 100 cc of water.) Second, spasm, which makes bladders so difficult to train, is very rare in conus or cauda lesions and common in higher lesions. Third, abdominal muscles are preserved in low lesions and aid in voiding. Fourth, the patient with a low lesion usually has a greater awareness of a full bladder which is an aid in bladder training.

TABLE 1. *Correlation of type of bladder with level of lesion*

	C.C.	INC. C.	C.D.	INC. D.	C.L.S.	INC. L.S.
Good neurogenic bladder (73)	3	9	21	1	14	25
Poor neurogenic bladder (69)	4	3	33	5	9	15
No trial (28)	12	2	8	0	3	3
	19	14	62	6	26	43

Where C.C.—Complete cervical; Inc. C.—Incomplete cervical
C.D.—Complete dorsal; Inc. D.—Incomplete dorsal
C.L.S.—Complete lumbosacral; Inc. L.S.—Incomplete lumbosacral

CORRELATION BETWEEN THE EARLY TREATMENT AND THE RESULTING TYPE OF BLADDER

A study of the past treatment of patients in the good and poor bladder groups has been made. As many of these patients have had the entire gamut of treatment so far as bladder drainage is concerned, it was necessary to formulate some arbitrary rules at the outset. It was decided to include only the type of bladder drainage used during the first 18 months of their paraplegic state, which is the maximum period of spinal shock. This decision was reached for two reasons. It seems logical to rationalize that if a bladder is properly drained from the onset of the injury, and if no complications such as a small contracted bladder, unhealed suprapubic or perineal sinus, urethral fistula or diverticulum develop, this bladder should be able to function at its maximum capacity after clinical spinal shock has ended. Secondly, it was recognized that some patients were permanently committed to urethral catheter drainage because of damage to the bladder by the early injudicious use of a suprapubic tube, and other patients were committed to suprapubic drainage because of complications arising from a urethral catheter. Therefore, if this is to be a fair comparison between the types of bladder drainage and the resulting function of the bladder, only the early period of treatment should be considered.

TABLE 2 *Type of bladder drainage*

	URETHRAL	PRED U	SP	PRED SP	MIS
Good bladders (73)	47	2	11	7	6*
Poor bladders (69)	28	5	9	24	3**
No trial (28)	—	—	—	—	

* 6 cases which developed good bladders required drainage for less than 1 month.

** 3 cases which developed poor bladders were treated by over flow incontinence.

The method of bladder drainage used during the first 18 months after injury was classified into four groups. One, solely suprapubic; two, solely urethral; three, predominantly suprapubic and four, predominantly urethral. Any period of drainage of less than one month was ignored.

We see that in 82 cases in which the bladder drainage employed during the first 18 months was either solely urethral catheter or predominantly by urethral catheter; good bladders developed in 49 (or 60 per cent) and poor bladders developed in 33 (or 40 per cent). Among 51 similar cases in which the early treatment was either by suprapubic catheter of predominantly by suprapubic catheter good bladders developed in 18 (or 35 per cent) and poor bladders developed in 33 (or 65 per cent).

ANALYSIS OF THE FACTORS RESPONSIBLE FOR THE DEVELOPMENT OF POOR NEUROGENIC BLADDERS

Many of the patients whose bladders are classified as poor clinically have achieved a reflex type bladder. The clinical standards set up for a good neurogenic bladder specify that the patient can retain his urine for at least 2 hours between voidings, and that during this period he will not leak urine. Therefore, in the group under consideration who have poor bladders clinically but still have a reflex type of bladder, are those whose voiding cycle is less than 2 hours. Also in this group are patients who could meet the 2 hour voiding cycle requirement, but any motion, coughing or sneezing, results in leakage of urine. Most of these patients do not require a catheter but must wear a rubber urinal at all times.

The 5 patients listed under the heading of retention have been paraplegics for more than 18 months but are still unable to empty their bladders without the use of a catheter. Their clinical picture is the same as spinal shock but they have passed the 18 month figure which is being used in this survey as the upper limits of duration of spinal shock.

Thirteen patients are totally incontinent (table 3). Most of this group describe their urination as a constant dribble. Others dribble urine at 5 to 10 minute intervals even after their bladders have been completely emptied.

An attempt will now be made to determine why these 69 cases developed poor bladders. The tools used include cystometric studies, clinical histories, bladder capacity and residual urine determinations, cystogram, cystoscopies, and an estimate of the degree of peripheral muscle spasm.

TABLE 3 *Analysis of poor neurogenic bladders*

Poor neurogenic bladders			(69)
Poor reflex bladders		51	
Short voiding cycle	35		
Leak urine	16		
Total retention		5	
Incontinence		13	

The cystometric studies (which were performed on 146 of the 170 patients) were done in the *manner* described by Mullenix. While this method is admittedly not as good as that described by Munro and Lewis for a scientific study of the bladder, it does give information concerning bladder capacity, bladder distensibility and reflex contractions and it is superior to other methods in determining the ability of the bladder to empty.

Bladder capacities and residuals were carried out from one to several times on all patients in the poor bladder group and on most patients in the good bladder group.

Cystoscopic examinations and cystograms were performed when indicated.

In working with these patients one becomes more and more impressed with the role played by spasm in distorting the normal cycle of the neurogenic bladder. All the patients in this series were graded on the basis of no spasm, mild, moderate, or severe by representatives of three services (G.U., Cord Injury and P. Medicine) who work intimately with these cases. This grading is of peripheral spasm, not bladder spasm.

After considering each case in the light of the above listed information, table 4 is submitted concerning the underlying reasons for the failure to develop better bladders. In many cases there are several factors involved in this failure.

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It is seen from table 4 that the failure to develop better bladders is attributed to spasm in 31 cases. These cases all give the clinical picture of voiding at frequent intervals; some every 15 to 20 minutes, others up to 1½ hours. Their voiding habits are unpredictable and do not follow a definite cycle in most cases. Many will say that spasm kicks off their bladder before it has a chance to fill. On cystometric study it is noted that these bladders will suddenly contract after from 25 cc to 200 cc of fluid has been introduced. The contraction is usually severe enough to give a cystometric reading of over 100 cc water and often will cause the patient to void around the catheter. All of these 31 patients have moderate or severe peripheral spasm.

If it is true, as Scarff and Pool postulate, that the segment of cord distal to the injury is hyperirritable and that impulses reaching this hyperirritable segment of the cord may be transmitted throughout other parts of the distal segment, it would seem logical that the reflex arc of the bladder could be so stimulated and the detrusor muscle forced to contract with no regard for the degree of fullness of the bladder. It also offers an interesting explanation of the trigger mechanism occasionally observed in paraplegics where pinching the groin or striking the thigh results in contraction of the bladder. We feel that this type of spasm is a contributing factor in 31 of our 69 cases classified as poor bladders. Incidentally, in all of these cases the lesion is in either the cervical or dorsal cord as lesions below D12 rarely develop spasm.

TABLE 4. *Factors responsible for the development of poor neurgoenic bladder*

	SPASM	CONTRACTED BLADDER	HIGH RESID URINE	LACK OF COOP.	SURGERY	LEVEL OF LESION	LOWER TRACT COMPLI
Poor reflex bladders (51)	26	18	6	5	2	6	3
Retention (5)	2	0	5	0	0	0	0
Incontinent (13)	3	4	0	0	3	6	0
Total	31	22	11	5	5	12	3

In 22 cases a small contracted bladder was considered to be the contributing factor in the resulting poor bladder. All of these cases have a bladder capacity of under 200 cc. In about 60 per cent of these contracted bladders peripheral spasm was an associated finding.

In 11 cases inability to satisfactorily empty the bladder is a factor in the bladder being classified as poor. All of these cases are out of spinal shock but still cannot void without a large residual urine. Five of these go into complete retention with each voiding test. The other 6 can express some urine and may void without a catheter for a while but invariably they lapse back either into complete retention or carry such a high residual that the catheter must be reinserted. Nine of these 11 have had at least one transurethral resection; 3 have had two and 1 has had three transurethral resections. Oddly enough, the lesion in all of these cases is above D11.

Twelve cases are believed to have failed because of the intrinsic nature and position of the cord injury. All of them present the clinical picture of incontinence of varying degrees. Six of them are almost completely incontinent, while 6 with reflex bladders are considered poor because of leakage of urine throughout the voiding cycle. All of these patients have a bladder capacity of over 200 cc and in none of them is spasm a factor. All have a cord lesion either in the conus medullaris or in the cauda equina. It is believed that flaccid paralysis of the external sphincter due to injury of the internal pudendal nerve or its reflex center could be the factor causing their incontinence.

In 3 cases failure to achieve a better bladder is traceable to lower tract complications. To these 3 should be added the 7 cases in which lower tract complications have rendered it impossible to ever have a voiding trial. These complications include peri-urethral abscess and its sequelae, urethral fistula and urethral diverticulum. Five of these 10 cases are war time injuries. On our own service where only small (16–18F) soft rubber Foley catheters are used and where the catheter can be cared for by trained technicians, these lower tract complications are becoming less and less frequent.

ANATOMICAL AND FUNCTIONAL CHANGES IN THE UPPER URINARY TRACT

In the paraplegic patient there are 3 great enemies of the upper urinary tract: infection, stones and reflux. The damage done by these are manifest by the dilatation of the upper urinary tract and by the gradual decrease of function both of which may be demonstrated by excretory urography. In an attempt to relate these anatomical and functional changes with the passage of time, 743 excretory pyelograms were reviewed. In recognition of the fact that an upper urinary tract which to one observer appears dilated may be considered normal by another, all films were read by one of us. In this way, we hoped to add a certain consistency to the interpretation. These pyelograms were classified as to the length of time elapsing between the date of injury and the date of the pyelogram to the closest six month interval.

It was difficult to find an accurate way to evaluate lost renal function (fig. 1). Functionally, the kidneys were classified as excellent, if contrast medium could be seen in the 5-minute film; good, if it was first seen in the 15 minute film; fair, if it was first seen in the 30 minute film and poor if no function could be detected. To arrive at some method of portraying these findings in chart form, any kidney classified as good was considered 1, fair 2 and poor 3. It was possible to arrive at a number to indicate the composite of the number of damaged kidneys and the degree of damage. This number was divided by the number of kidneys examined and an arbitrary figure which increases as the loss of function increases was reached. If, for example, all the kidneys examined pyelographically at 6 months showed excellent function the figure would be zero (.000). As more kidneys were examined which had impaired function, this index would increase.

Reflux cannot be measured by the pyelogram but requires a cystogram. Routine cystograms were not done but were ordered on all cases in which severe hydro-ureter and hydronephrosis were present. Had cystograms been performed on all cases, the incidence would undoubtedly be greater than is reported here. With these notes of explanation the graph should be more easily understood.

Anatomical dilation of the upper urinary tract shows a gradual increase during the first 18 to 24 months and then continues on at a constant rate. The relationship maintained between the three components (calyectasis, hydronephrosis and hydro-ureter) is very interesting. Dilatation of the calyx is consistently the most prevalent. Many of these kidneys are the site of chronic and acute pyelonephritis which is revealed pyelographically by calyectasis without dilatation of the renal pelvis or the ureter. In second place is hydro-ureter which is consistently a few percentage points more prevalent than hydronephrosis. It has been our impression from observing these pyelograms that the dilatation of the collecting system (renal pelvis and ureter) begins in the lower part of the ureter and advances upward to include the renal pelvis. This slight prevalence of hydro-ureter over hydronephrosis is confirmatory.

GRAPHIC PORTRAYAL OF UPPER URINARY TRACT PATHOLOGY IN ENTIRE SERIES (170 PATIENTS)

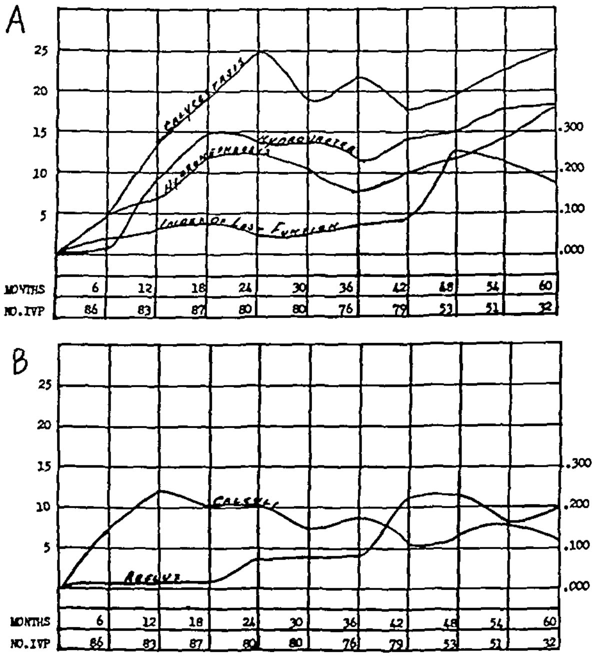

FIG. 1. *A*, percentage of patients showing calycectasis, hydro-ureter, hydronephrosis and index of lost renal function with special scale calibrated on right. *B*, percentage of patients showing reflux and calculi.

We see, therefore, that the anatomical changes occurring in the upper urinary tract tend to level off after gradually rising for the first 18 to 24 months. What is happening to the renal function? Here we note a very gradual but persistent rise in functional loss from the onset of injury through the 42 month (3½ years) period. There is a sharp rise in the index of function loss at 48 months which is maintained at 54 months and drops only slightly at 60 months. One is impressed by the fact that while the anatomical changes have leveled off the degree of functional loss is progressing.

What part do the causative agents play in producing this picture? First, there is infection which is almost universally present in these cases. It has been pointed out that this is probably the factor which makes calyectasis the most common anatomical change. It is difficult to get an accurate record of past attacks of acute pyelonephritis. One must rely on the history of chills and fever which may or may not have been a true acute pyelonephritis. Also, a patient's memory is unreliable when asked about "kidney flare-ups" which occurred some years before. In questioning these 170 patients we were impressed with the great number who had "kidney flare-ups" frequently in the first year or two of their disease but had them only rarely as times passed. We formed the opinion that acute pyelonephritis was much more frequent early in the course of the disease and was relatively infrequent after the first two years. This is logical since most of them have had the catheter removed during the first two years and no longer have a foreign body in their urinary tract. We believe that these anatomical changes would continue to progress as does the function loss if it weren't for the decrease in prevalence of infection after the second year.

GRAPHIC PORTRAYAL OF UPPER URINARY TRACT PATHOLOGY IN THE 73 PATIENTS WHO HAD GOOD NEUROGENIC BLADDERS.

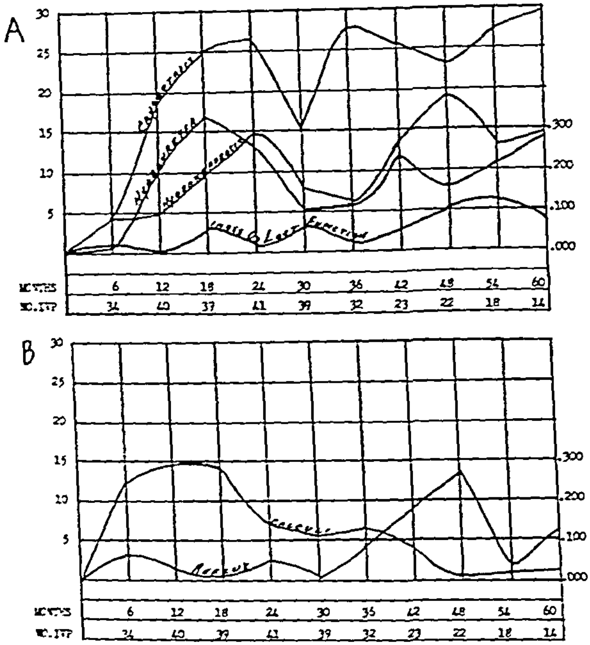

FIG. 2. *A*, percentage of patients showing calyceectasis, hydro-ureter, hydronephrosis and index of lost renal function with special scale calibrated on right. *B*, percentage of patients showing reflux and calculi.

Infection is, of course, a major factor in the formation of calculi which brings us to that second causative agent. Any patient with a recent cord injury is fair game for the formation of urinary calculi. He has an infected urinary tract, he is immobilized, and he often has several fractured bones. As would be expected it is in the early part of the disease that calculi formation is at its height. The percentage of stones in the late months do not represent new stone formation but rather old stones which have been allowed to remain in the kidney either because they are small and not obstructing or because they cannot be removed safely for one reason or another.

Certainly calculus disease, along with infection, has accounted for much of the early anatomical changes noted in these patients. However, it is difficult to attribute the sharp rise in loss of function noted in the 48 and 54 months since this late in the course of the disease stone formation and infection are on the decrease.

GRAPHIC PORTRAYAL OF UPPER URINARY TRACT PATHOLOGY IN THE 69 PATIENTS WHO HAD POOR NEUROGENIC BLADDERS.

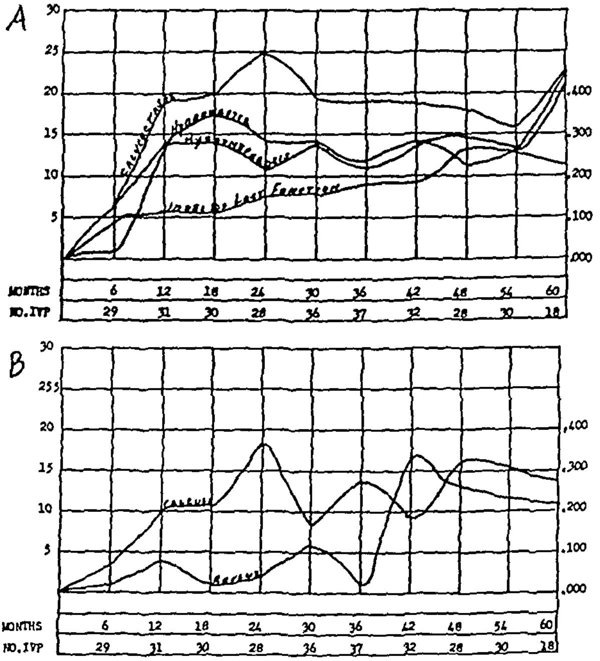

FIG. 3. *A*, percentage of patients showing calyectasis, hydro-ureter, hydronephrosis and index of lost renal function with special scale calibrated on right. *B*, percentage of patients showing reflux and calculi.

This brings us to the third factor, reflux. Reflux has been gradually rising throughout the first 3 years, but it has never been greater than 5 per cent until the 42 month period when it is noted in 13 per cent of the cases studied. This percentage is maintained at 48 months but drops off slightly at 54 months and is rising again at 60 months. As was mentioned earlier there is probably more reflux than recorded since only selected cases were studied with cystograms. It is striking that this increase in reflux should coincide so closely with the sharp rise in loss of renal function noted at 48, 54 and 60 months. We believe that while much of the anatomical changes noted as hydro-ureter, hydronephrosis and calyectasis are due to infection and calculi, part of it must be the precursor of frank ureteropelvic reflux. We also believe that reflux is a great destroyer of renal tissue in the later stages of the paraplegic state.

COMPARISON OF THE UPPER URINARY TRACTS OF PATIENTS WITH CLINICALLY GOOD BLADDERS AND WITH CLINICALLY POOR BLADDERS

It has been our clinical impression that those paraplegics whose bladders were good have less upper urinary tract complications. In an effort to confirm or deny this hypothesis, figure 1 has been broken down so that the upper urinary tract disease of the good and poor bladder groups could be analyzed separately and compared.

Careful study of these graphs shows that the percentage of calyectasis, hydroureter and hydronephrosis is about the same in each group. However, the incidence of renal and ureteral calculus and of reflux is definitely higher in those paraplegics with poor bladders. Probably of even greater significance is the index of lost renal function which is much higher in the poor bladder group.

We believe that this comparison tends to confirm the generalization that "in paraplegics as the bladder goes, so go the kidneys." This, however, is only a generalization because as figure 2 illustrates, many patients whose bladders are clinically good are undergoing severe renal damage.

SUMMARY AND CONCLUSIONS

This study is based on data collected from 170 paraplegic patients. Eighty-five (or 50 per cent) of these patients received their injuries during or before World War II. The group averages 4.04 years since injury.

Clinically good neurogenic bladders have developed in 63 per cent of the cervical injuries, 37 per cent of the dorsal injuries and 62 per cent of the lumbosacral lesions.

Sixty per cent of the patients whose bladders were drained by urethral catheters during the period of spinal shock eventually developed clinically good bladders. In a similar group whose bladders were drained by suprapubic catheters only 35 per cent developed clinically good bladders. It was concluded that urethral drainage offers a better opportunity for bladder recovery than does suprapubic drainage. Factors responsible for the failure of the paralyzed bladder to regain its function were analyzed. Spasm and contracted bladders were the most common causes for this failure. Other factors included incontinence, complete or partial retention and lower urinary tract complications.

A study of the changes occurring in the upper urinary tracts of paraplegic patients with the passage of time was undertaken. It was found that anatomical changes as judged by hydronephrosis, hydro-ureter and calyectasis rose rapidly during the first 24 months and then tend to level off. Functional damage as judged by excretory urography is not marked during the first 3 years and then increases rapidly. Causative factors such as stones and infection are more marked during the first 2 years and then become less and less of a factor. The curve plotting their incidence follows closely the curves denoting anatomical damage to the kidneys and ureter. On the other hand, the incidence of vesical ureteral *reflux is not great until the end of the third year and then it rises sharply, paralleling closely the curve denoting loss of renal function. It was also noted that more damage to the upper urinary tract occurs in patients whose bladders function poorly.*

REFERENCES

ABRAMSON, D. J.: Urologic problems of spinal cord injury. J. Urol., **61**: 479–486, 1948.

BORS, E.: Spinal cord injuries, Veterans Administration Technical Bulletin (TB10-503) December 15, 1948.

BOYD, M. L.: Suprapubic drainage in bladder paralysis. J. Urol., **60**: 922–933, 1948.

BUMPUS, H. C., JR.: Transurethral resection and the paraplegic. J. Urol., **57**: 300–303, 1947.

DONOVAN, H.: Care of the urinary tract in paraplegic patients. Lancet, 1: 515–518, 1947.

EMMETT, J. L.: Urinary retention from imbalance of the detrusor and vesical neck. J. Urol., **43**: 692–704, 1940.

HUGGINS, C., WALKER, A. E. AND NOONAN, W. J.: Sympathetic and pudendal neurectomy for vesical atony. J. Urol., **41**: 696–714, 1939.

JACOBSON, C. E., JR.: Neurogenic vesical dysfunction. J. Urol., **54**: 670–695, 1945.

KIMBROUGH, J. C.: Urology in the European Theater World War II. J. Urol., **57**: 1105–1116, 1947.

LEWIS, L. G.: Treatment of bladder dysfunction after neurologic trauma. J. Urol., **54**: 284–295, 1945.

MARTIN, J. AND DAVIS, L.: Studies upon spinal cord injuries. Ann. Surg., **126**: 472–477, 1947.

MUNRO, D.: Treatment of urinary bladder in cases with injury of the spinal cord, Am. J. Surg., **38**: 120–136, 1937.

MULLENIX, R. B.: Cystometry in the study of traumatic neurogenic bladder. J. Urol., **55**: 470–482, 1946.

NESBIT, R. M., ET AL.: The effects of blockade of the autonomic ganglia of the urinary bladder in man. J. Urol., **57**: 242–250, 1947.

NOURSE, M. N. AND BUMPUS, H. C.: Care of the paraplegic's urinary tract. J. Urol., **57**: 495–497, 1947.

PATE, V. A. AND BUNTS, R. C.: Peritonitis from suprapubic sinus. J. Urol., **60**: 915–922, 1948.

PETROFF, B. P.: War wounds of the spinal cord. J.A.M.A., **129**: 154–155, 1945.

PRATHER, G. C.: Urological Aspects of Spinal Cord Injuries. Springfield, Ill.; C. C. Thomas, publisher, 1949.

PRATHER, G. C. AND PETROFF, B P.: Spinal cord injuries: Urethrographic study of the bladder neck. J. Urol., **57**: 274–284, 1947.

SCARFF, J. E. AND POOLE, J. E.: Factors causing massive spasm following transection of the cord in man. J. Neurosurg., **3**: 285–293, 1946.

✓ TALBOT, H. S.: Cystometry and the treatment of vesical dysfunction in paraplegia. J. Urol., **59**: 1131–1147, 1948.

TALBOT, H. S. AND BUNTS, R. C.: Late renal changes in paraplegia. J. Urol., **61**: 870–880, 1949.

TALBOT, H. S., LYONS, M. K. AND BASSELL, A. J.: The major urologic considerations in paraplegia. New Eng. J. Med., **241**: 259–262, 1949.

THOMSON-WALKER, SIR J. W.: The bladder in gunshot and other injuries of the spinal cord. Lancet, **1**: 173–179, 1917.

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MALAKOPLAKIA OF URINARY BLADDER AND SARCOIDOSIS

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Malakoplakia (Gr., soft plaque) is a rare disease which is characterized by soft, yellowish gray plaques of varying sizes on the mucosa of the urinary bladder. The patches usually are surrounded by a zone of hyperemia and may be elevated. The condition occurs more frequently in women than in men, and may affect the ureters, renal pelvis, and renal parenchyma.[1] Frequency of urination is the most prominent symptom and hematuria may be present. The lesion is inflammatory and is thought to represent a variety of chronic cystitis. The resemblance to tuberculous lesions has been noted, but no specific etiologic agent has been demonstrated. The prognosis is excellent for, as in sarcoidosis, spontaneous regression is the rule.

Morison[2] collected approximately 50 cases of malakoplakia from the literature in 1944, and most of these had been confirmed by biopsy. The association of comparable lesions in the urinary bladder and in the skin led Redewill[3, 4] to classify malakoplakia of the urinary bladder as a manifestation of sarcoidosis. But most of the case reports of malakoplakia did not include reference to cutaneous sarcoidosis. Michaelis and Gutmann[5] in 1902 described characteristic refractile bodies in malakoplakia, which von Hansemann[6] in 1903 designated as Michaelis-Gutmann bodies. Wells[7] reported calcospherites in cystitis with giant cells. Other articles of interest include those of Cristol and Broders,[8] Pappenheimer,[9] and Rudnick and Ragins.[10]

We have an additional case to report in which typical lesions of malakoplakia were present in the urinary bladder and equally typical changes of sarcoidosis were found in the skin.

CASE REPORT

A 41 year old Negress was admitted to the University Hospital on November 14, 1948, complaining of "lumps" in the skin. She had been well until February 1948, when she became dizzy and fainted while working at her home. She had not fainted subsequently, but frequently had vomited food and bile. The first skin lesions were noted on the arms, and the skin over the lesions became depigmented. At the time of hospitalization she had lesions over her arms, legs, buttocks, abdomen, and face. They increased in size, and then dried in the central portions and became flatter. No fluid or purulent exudate was present in the lesions. None of them completely disappeared, and while slightly pruritic they were not tender unless traumatized. If traumatized, the pain that resulted was like that which results from stimulation of the ulnar nerve.

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[1] McDonald, S. and Sewell, W. T.: Malakoplakia of the bladder and kidneys. J. Path. & Bact., 18: 306–318, 1913–14.

[2] Morison, J. E.: Malakoplakia of the urinary bladder. J. Path. & Bact., 56: 67–72, 1944.

[3] Redewill, F. H.: Malakoplakia of the urinary bladder and generalized sarcoidosis. J. Urol., 49: 401–407, 1943.

[4] Redewill, F. H.: Comparison of leukoplakia, malakoplakia, and incrusted cystitis. J.A.M.A., 92: 532–536, 1929.

[5] Michaelis, L. and Gutmann, C.: Ueber Einschlüsse in Blasentumoren. Ztschr. f. klin. Med., 47: 208–215, 1902.

[6] von Hansemann: Über Malakoplakie der Harnblase. Virchows Arch. f. path. Anat., 173: 302–308, 1903.

[7] Wells, H. G.: Giant cells in cystitis. Arch. Path., 26: 32–43, 1938.

[8] Cristol, D. S. and Broders, A. C.: Malacoplakia of the bladder. J. Urol., 55: 200–206, 1946.

[9] Pappenheimer, A. M.: Malakoplakia of the urinary bladder. Proc. New York Path. Soc., 6: 65–71, 1906.

[10] Rudnick, D. F. and Ragins, A. B.: Malakoplakia of the bladder. J. Urol., 42: 108–117, 1939.

In March 1948, urination had increased to 10 to 15 times a day and 6 to 7 times a night, with an occasional episode of urgency and incontinence. With urination she had terminal pain at the urethral orifice and gross blood was present in the urine. Low, dull backache, and edema of the feet and ankles occurred at the end of a day of standing. She had noted shortness of breath from the onset of the present illness. Menstruation had occurred only twice since February 1948, and she then had no pain with the menses, whereas dysmenorrhea had been a usual complaint.

Physical examination revealed an obese patient who did not appear ill. The pulse rate was 64 per minute; the blood pressure was 108 mm. of mercury systolic and 68 diastolic; and the respiratory rate was 20 per minute. The liver was palpated 10 cm. below the right costal margin, and the spleen was felt 6 cm. below the left costal margin. Tenderness was elicited by palpation over the region of the urinary bladder. Several firm, slightly tender, medium-sized lymph nodes were palpated in the anterior region of the neck and beneath the angles of the mandible. Smaller lymph nodes were detected in the axillae. The extensor surfaces of the arms, forearms, and thighs, the posterior surfaces of the legs, the buttocks, the abdomen, and the face contained skin lesions. The more recent ones were soft, slightly raised, depigmented areas, less than 1 cm. in diameter, with irregular borders.

Laboratory data of significance included a report of the tuberculin test which was negative in a dilution of 1:10,000 O.T., at 24 and 48 hours. However, 10 days later in a dilution of 1:1,000 O.T., the tuberculin skin test was positive at 24 and 48 hours. Repeated direct examinations of sputum, 24-hour, 48-hour, and 3-day specimens, and gastric aspirations were negative for acid-fast organisms. Animals inoculated with urine did not develop tubercles. Microscopic sections of the skin showed granulomatous lesions characteristic of sarcoidosis of Boeck. The sedimentation rate was 33 mm. per hour. Serum globulin was 5.6 gm. per cent, and serum albumin was 3.6 gm. per cent, giving total serum proteins of 9.2 gm. per cent. The blood Kahn test was negative.

X-ray films of the skull and bones of the extremities were negative. Extensive pulmonary abnormalities were interpreted as being compatible with a diagnosis of sarcoidosis.

The urinary frequency decreased with sulamyd and calcium therapy, and the patient was discharged from the hospital on December 6, 1948, to be followed in the Outpatient Clinic.

The urinary bladder was described by the cystoscopist as being "studded with flat, light gray nodules between which the mucosa was normal." The minute fragments of tissue submitted for microscopic examination on two occasions were similar and both showed changes characteristic of malakoplakia (fig. 1, *A* and *B*).

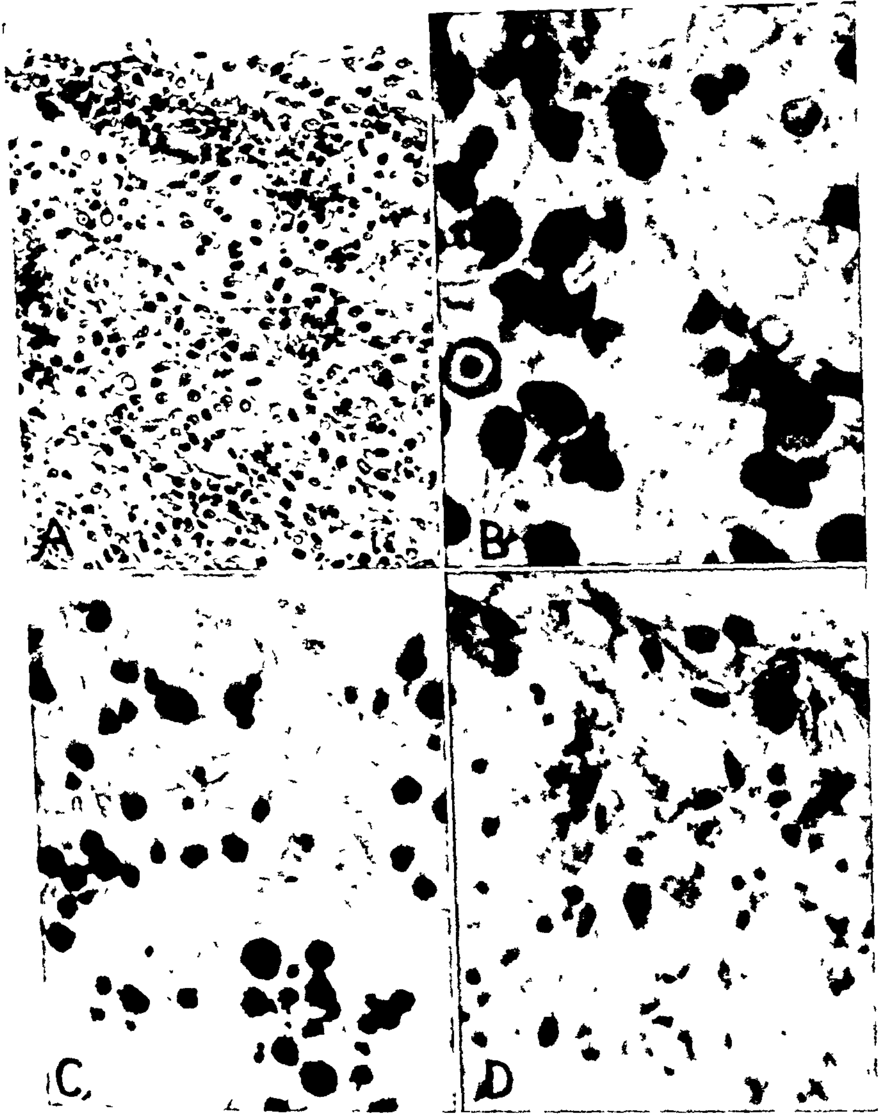

Fig. 1. *A*, mucosa of urinary bladder showing Michaelis-Gutmann bodies. Hematoxylin and eosin stain. × 100 *B*, Michaelis-Gutmann bodies in bladder mucosa. Hematoxylin and eosin stain. × 430. *C*, Von Kossa's stain showing phosphate and, indirectly, calcium content of Michaelis Gutmann bodies × 430. *D*, Gomori's stain showing presence of iron in Michaelis-Gutmann bodies in urinary bladder. × 430.

Minute granules, Michaelis-Gutmann bodies, were present in and between not fainted subsequently, but frequently had vomited food and bile. The first skin lesions were noted on the arms, and the skin over the lesions became depigmented. At the time of hospitalization she had lesions over her arms, legs, buttocks, abdomen, and face. They increased in size, and then dried in the central portions and became flatter. No fluid or purulent exudate was present in the lesions. None of them completely disappeared, and while slightly pruritic they were not tender unless traumatized. If traumatized, the pain that resulted was like that which results from stimulation of the ulnar nerve.

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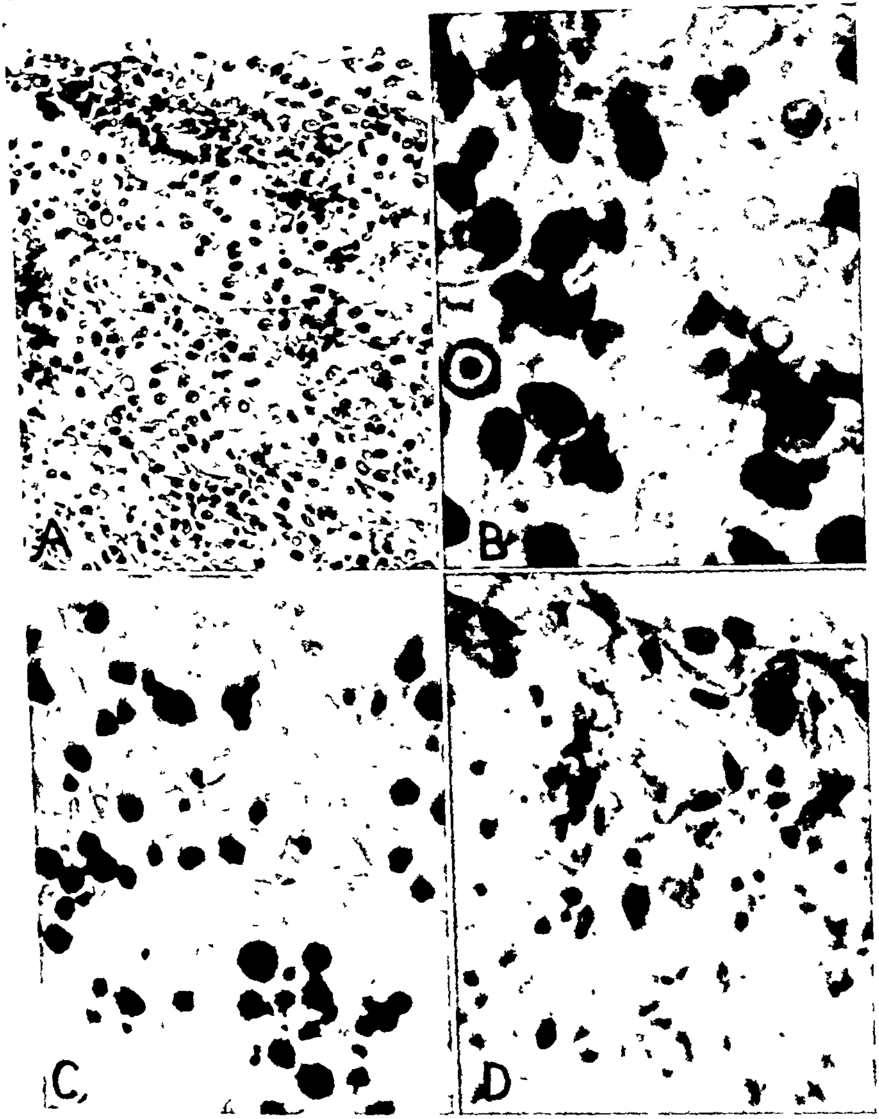

FIG. 1. *A*, mucosa of urinary bladder showing Michaelis-Gutmann bodies. Hematoxylin and eosin stain × 100. *B*, Michaelis-Gutmann bodies in bladder mucosa. Hematoxylin and eosin stain × 430. *C*, Von Kossa's stain showing phosphate and, indirectly, calcium content of Michaelis-Gutmann bodies. × 430. *D*, Gomori's stain showing presence of iron in Michaelis-Gutmann bodies in urinary bladder. × 430.

were similar and both showed changes characteristic of malakoplakia (fig. 1, *A* and *B*).

Minute granules, Michaelis-Gutmann bodies, were present in and between epithelioid phagocytic cells. Some of the bodies were laminated granules but the larger ones were round objects which resembled corpora amylacea of the lungs or prostate, so-called psammoma bodies or "brain sand" in the meninges, or calcospherites in some ovarian and other carcinomas.

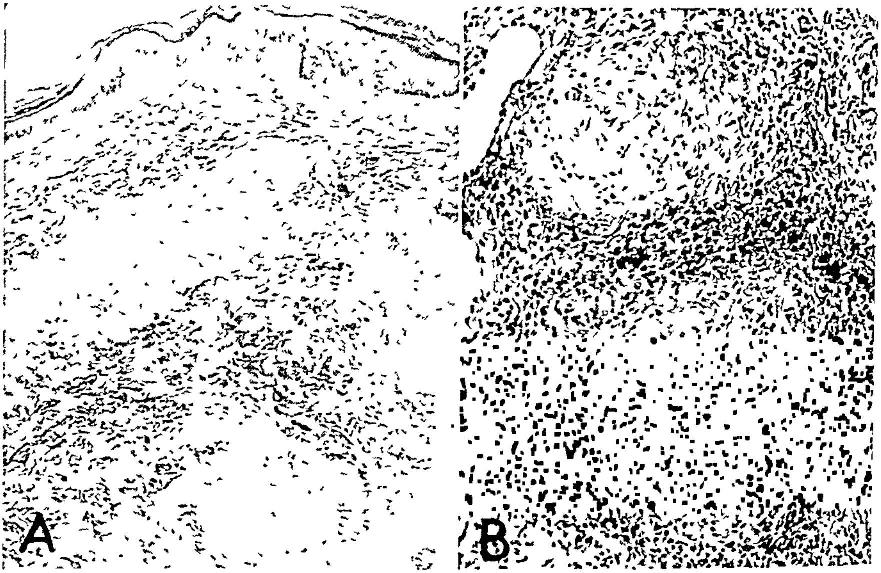

Fig. 2. *A*, sarcoidosis of skin, from the same patient, with noncaseous epithelioid tubercles in dermis. × 25. *B*, epithelioid tubercles in dermis. Sarcoidosis. × 100.

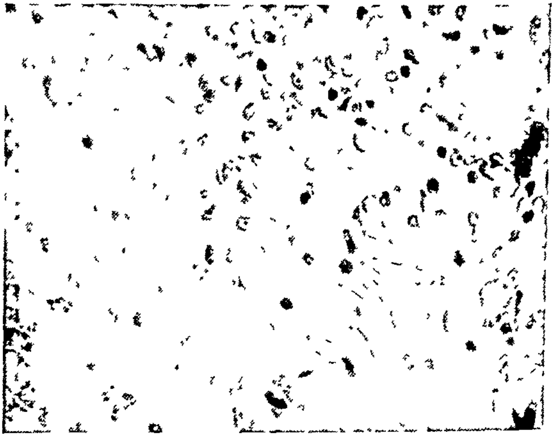

Fig. 3. Sarcoidosis Dermal-epidermal junction with Langhans' giant cell and pigmentation of epidermis. × 430.

The Michaelis-Gutmann bodies, measured by a calibrated micrometric disk, varied in size from 2 to 10 μ in diameter. The larger examples appeared distinctly laminated after staining with hematoxylin and eosin. In the bladder wall the bodies were more numerous near the mucosa than toward the muscularis. They occurred in large monocytes with foamy or granular cytoplasm and pyknotic polymorphous nuclei. More than one body might be present in a single cell. Polymorphonuclear leukocytes were abundant in the capillaries but lymphocytes were not prominent. The bodies were stained best by the von Kossa method (fig. 1, *C*) for phosphate which, at the same time, indicates the presence of calcium in combination. As shown by this method, a few bodies were present in superficial portions of the bladder wall, but most of them were concentrated near the mucosa.

Gomori's iron reaction (fig. 1, *D*) demonstrated hemosiderin or other stainable iron in less than one-half of the bodies present. While no constant pattern was detectable, the bodies in the deeper portions of the tissue tended to give the iron reaction more uniformly and more constantly than those nearer the mucosa. No constant difference in size of stainable bodies was noted, but the larger bodies did contain a dense core or nidus which stained a deep scarlet with basic fuchsin. The laminated pattern seen in hematoxylin- and eosin-stained material was not evident in the von Kossa or Gomori preparations.

The dermis contained sheets of epithelioid tubercles (fig. 2) with little or no caseation necrosis. The epithelioid cells here were somewhat comparable to the phagocytic cells in the lesions in the urinary bladder. A few Langhans' giant cells (fig. 3) were present at the periphery of the tubercles in the skin lesions. Partial depigmentation of the basal cell layer of the skin was noted. Stains for acid-fast organisms were negative on the specimens of the skin and of the urinary bladder. The skin lesion was considered characteristic of sarcoidosis.

SUMMARY

An additional case of sarcoidosis of the skin and concomitant malakoplakia of the urinary bladder is added to the 2 similar cases reported by Redewill.[3] Clinical and histopathologic findings were comparable to those in his cases. Malakoplakia of the bladder and cutaneous sarcoidosis are both relatively rare conditions. Their concomitance is believed to be more frequent than would be expected under free chance distribution. This implies some common etiologic factor.

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AN OPERATION FOR THE CURE OF TOTAL URINARY INCONTINENCE IN THE MALE: REPORT OF ONE CASE

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One of the most distressing conditions presented to the urologist is that of the totally incontinent patient. It becomes of even more paramount importance when it is learned such a state has resulted from operative procedures designed to rid the patient of symptoms which to him seemed minor compared to the deplorable state of constant urinary leakage. The technique about to be described is in the nature of a preliminary report which hitherto had not been applied to the totally incontinent male.

The idea of the combined use of an abdominal fascial aponeurotic sling and reconstruction of the urogenital diaphragm was suggested in part by the many excellent results on urinary stress incontinence in women secured by elevation of the floor of the bladder by means of fascial strips such as described by Meigs, TeLinde, Marshall and others. The late Dr. Hugh Young noted remarkably good results in 3 of 5 cases rendered incontinent by surgical procedures. His technique consisted of re-approximation of the external sphincter and narrowing of the internal vesical orifice.

The literature contains but few references to procedures designed for correction of total incontinence in the male. In 1911, J. Bentley Squier reported a successful result by narrowing the urethra and re-approximating the transversus perinei and levator ani muscles. Three years later Frangenheim reported a successful result in which the fascial sling principle was applied. The pyramidalis muscle with an attached strip of rectus fascia was brought down retropubically to encircle the urethra.

More recently Dr. Vergés-Flaqué has reported marvelous results in 5 cases in which a portion of the external anal sphincter is used to encircle the bulbous urethra.

Our case (R. B. Reg. No. 55870 V. F. G. H.) was a 52 year old veteran admitted to Valley Forge General Hospital in June 1949, totally incontinent of urine the result of a transurethral resection performed elsewhere 1 month previously. He was unable to retain any urine in either the erect or recumbent posture. Panendoscopic examination demonstrated a very adequately resected internal vesical orifice and prostatic fossa. As the instrument was withdrawn a distinct asymmetry of the external sphincter was at once apparent. The normal iris-like diaphragm had been converted into a racquet shaped opening due to a deep defect at 7 o'clock. Bladder contour was normal as demonstrated by cystogram. Expulsive force was good. The urine was clear and microscopically nega-

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Read at annual meeting, Northeastern Section, American Urological Association, Bolton Landing, N. Y., September 14, 1950.

tive. Serologic test for syphilis was negative. There was no doubt but that the incontinence was entirely on the basis of operative damage to the sphincter mechanism.

TECHNIQUE

A transverse semicircular incision was made in the lower abdominal wall coursing just above the symphysis pubis which exposed the deep fascia. Fascial strips 1 cm. wide and 15 cm. long were raised from the aponeurosis of the external oblique and rectus abdominis muscles in the direction of the fascial fibers. Each remained attached at its lower end just above the symphysis and approximately 2.5 cm. from the linea alba. The defect created was closed by approximation of the fascia except for a small hiatus at the lowermost end. Entrance to the space of Retzius was gained by a separate, small transverse incision approximately 5 cm. above and directly between the incisions used for development of the flaps. Cleavage on either side of the bladder and lateral aspects of the prostate was developed by blunt dissection. A tunnel through the fascia overlying the rectus muscle and then lateral to each rectus muscle was created on either side to permit the introduction of the fascial strips into the subsymphyseal space. The patient was then placed in exaggerated lithotomy position and the usual perineal exposure as for perineal prostatectomy was carried out until the membranous urethra and prostate were exposed. The prostate was found to be quite small, the surgical capsule being approximately ⅛ inch in thickness. There was no clear cut urethroprostatic junction. More extensive dissection than is customary in perineal prostatectomy was performed so as to fully uncover the urogenital diaphragm and expose region of the scar resulting from division of the external sphincter. Identification of this area was facilitated by palpation against the urethral sound. With an assistant working from above, the fascial flaps previously raised were guided subsymphyseally through the lateral prostatic space, care being taken to hug the symphysis closely to avoid injury to the venous plexus. The flaps could then be crossed at the membranoprostatic juncture causing a marked upward angulation of the urethra.

Reconstruction of the urogenital diaphragm was completed before anastomosis of the fascial flaps. The scar in the diaphragm, palpated against the sound, was widely excised along with a generous portion of membranous urethra. A 5F ureteral catheter was threaded through the urethra and directed into the bladder. The urethra was closed and narrowed by a continuous suture of 4-0 chromic catgut. The exposed edges of urogenital diaphragm were approximated in the midline by multiple sutures of chromic 1 catgut, care being taken to secure generous bites of muscle on either side. The fascial flaps were then crossed at the membranoprostatic juncture and pulled sufficiently snug to give a pronounced elevation and angulation to this region. The sling was completed by tying the ends into a square knot and fixing it by chromic 1 catgut suture directly through the knot. The perineum was closed in routine fashion, a Penrose drain having been placed in the wound.

Urinary drainage was provided by suprapubic cystostomy.

The perineal drain was removed after 5 days. Convalescence was complicated by the development of wound infection in the cystostomy incision and intermittent perineal urinary leakage which persisted for approximately 2 weeks. Fortunately there was no fascial slough or breakdown of the wound. From time to time some urinary leakage occurred about the small splinting urethral catheter. The splinting catheter was removed 29 days following operation. The bladder was filled through the suprapubic tube and it was found that the patient could retain 250 cc urine. He was able, but with difficulty, to stop and start the urinary stream at will. The suprapubic tube was removed and the fistula closed within 2 days. Urinary control was at first quite imperfect with loss of urine on exertion between interval voids of 100 to 200 cc. He was given active exercise of the abdominal muscles and static gluteal exercises. There was progressive improvement in control until the patient was able to retain as much as 725 cc urine and to void with good control except for the loss of an occasional few drops of urine on sudden cough. He was discharged September 1949.

Re-examination 1 and then 11 months later demonstrated no stricture. The urethra calibrated at 24F. With the panendoscope a definite angulation at the membranoprostatic was readily apparent. The external sphincter region appeared puckered, the original defect having been obliterated. The urine was clear. Control can be considered as good except that at full capacity there is loss of a few drops of urine on vigorous exertion.

DISCUSSION

The authors are aware that this constitutes but a single case result. The technique has been described with the hope that others may make use of the procedure and report their findings. It is difficult to ascertain whether or not control could have been secured by simple suspension with the fascial sling without the extensive dissection and re-approximation of the urogenital diaphragm. The recent report by Ewert et al. on the use of rectus muscle sling alone for neurogenic incontinence would lead one to believe it might certainly be possible. From the panendoscopic appearance following operation, one is made to believe that the marked angulation of the urethra produced by the sling is the chief factor in affording the increased urethral resistance necessary to provide continence.

SUMMARY

An operation designed to cure total urinary incontinence in the male is described in which the principles of abdominal fascial aponeurotic sling and reconstruction of the urogenital diaphragm are used. The patient was incontinent as a result of transurethral resection in which both internal and external sphincters had been divided.

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REFERENCES

Ewert, E. E. and Flint, L. D.: Rectus muscle sling for neurogenic incontinence. Surgery, 27: 688, 1950.

Frangenheim, C.: Zur Operativen Behandlung der Inkontinenz der Mannlichen Harnbröhre. Verhandlungen der deutschen Gesellschaft für Chirurgie, 43rd Congress, 1914.

Marshall, V. F., Marchetti, A. A. and Krantz, K. F.: Correction of stress incontinence by simple vesicourethral suspension. Surg., Gynec. & Obst., **88**: 509, 1949.

Meigs, J. V.: The fascial sling operation for incontinence of urine. J. Mt. Sinai Hosp., **14**: 504, 1947.

Squier, J. B.: Postoperative urinary incontinence; urethroplastic operation. Med. Rec., **79**: 868, 1911.

Young, H. H. and Davis, D. M.: Young's Practice of Urology. Philadelphia: W. B. Saunders Co., 1926.

Vergés-Flaqué, A.: Flaqué-Lowsley operation for urinary incontinence; Preliminary report. J. Urol., **65**: 427–437, 1951.

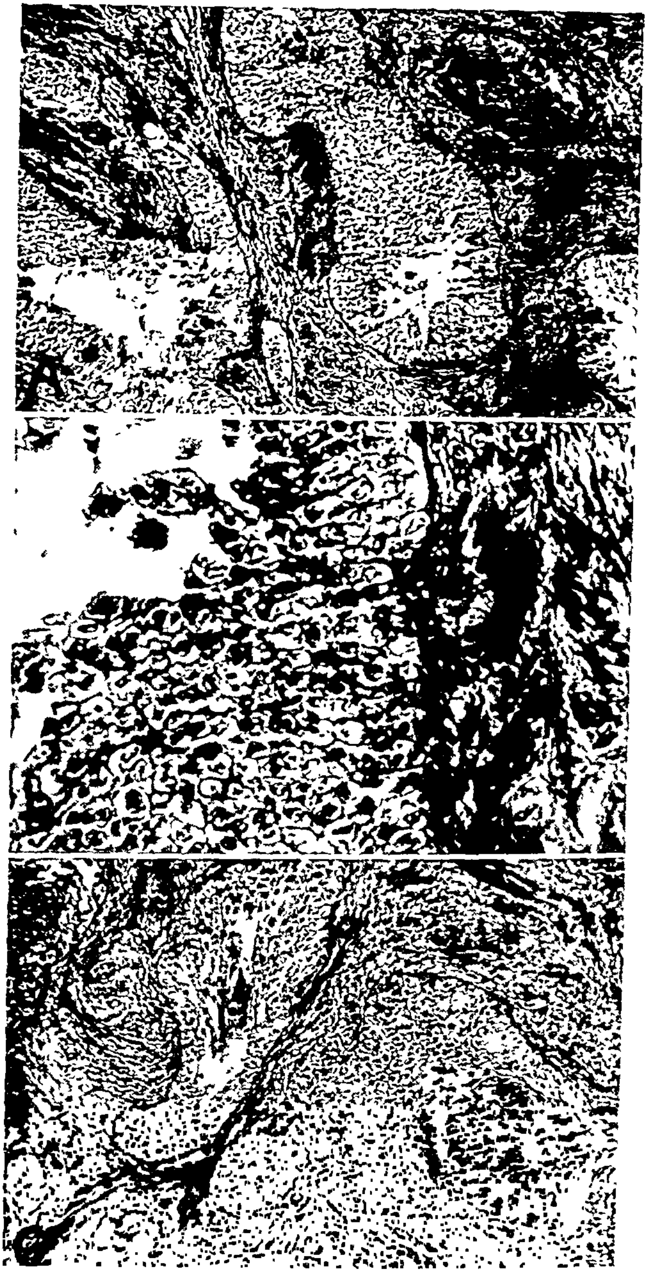

FIG. 1. *A*, biopsy taken from bladder which shows transitional cell carcinoma of the bladder. ×90. *B*, biopsy taken from bladder which shows transitional cell carcinoma of bladder. × 300. *C*, transitional cell carcinoma involving corpora cavernosa of penis. × 90.

surrounding tissue. The mass of tissue measures 3 by 2 by 1 cm. On cut section, the firm surface is rather thick measuring 3 mm. in thickness and is of a greyish white color.

"Specimen B consists of 2 testicles. One weighs 18 gm., the other weighs 17 gm. The external surface is smooth, shiny and of a dark, greyish pink color. The testicular tissue is soft to palpation. No nodules are felt. On cut surface, a stringy appearance is not present. The cut surface is slightly irregular but shiny and of a dark greyish pink color. The cut surface is also soft to palpation.

"Microscopic: The specimen reveals a transitional cell carcinoma invading the penis and essentially normal testes. The tumor is composed of transitional cells tending to grow from a stroma that has a papillary architecture. There are numerous irregular areas which are composed of columnar to polyhedral epithelial cells. These cells have a granular pink cytoplasm and deep staining nuclei with frequent mitotic figures. The tumor is moderately pleomorphic. There is a moderate infiltration of chronic and acute inflammatory cells (fig. 1).

"Sections of the testicles show the tubules to be normal and there is evidence of active spermatogenesis, which is a little unusual for a man of this age. The remaining section is not remarkable except the basement membrane is slightly thickened."

The patient is now very uncomfortable. He is having difficulty in emptying his bladder and carries a very dirty urine. He still has severe pain and burning on urination and is unable to get much rest either night or day. To date the lesion has not broken through the corpora but the patient is losing weight and his general condition seems to be deteriorating.

SUMMARY

This is the case of a patient who was found to have transitional cell carcinoma of the bladder with secondary metastasis to the corpora cavernosa of the penis.

This is a rare condition and no explanation is given or could be found for the manner in which this tumor metastasized to the penis.

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REFERENCE

WATTENBERG, C. A.: Unusual tumors and secondary carcinomas of the penis: Review of the literature and report of a case. J. Urol., 52: 169, 1944.

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STRICTURE OF THE FEMALE URETHRA

DORSEY BRANNAN

My attention has recently been focused on the subject of stricture of the female urethra because of a fatality resulting from this lesion (case 1). I believe that a condition which can ultimately lead to death and which as it appears, has not been particularly emphasized in urologic literature, merits some comment.

Another fatal case was reported in the German literature in 1920 by Heinrichsdorff: A woman aged 65 acquired an injury to the urethra during labor with a resulting urethrovaginal fistula. A severe stricture gradually developed over a period of years which ultimately led to the patient's death. She presented clinically the picture of sepsis and coma (uremia?) and died 3 days after admission to the hospital. The urinary bladder was found dilated as well as the ureters and renal pelves, with abscesses in the kidneys and also extensive infection of the entire urinary system and associated general sepsis.

Wynne, in his important contribution in 1927, referred to an article by Thompson in the English literature, who referred to another obvious fatal case of urethral stricture in the female. The report briefly described a museum specimen in the possession of the Royal College of Surgeons of Edinburg, of a 30 year old woman with strictured urethra, secondary changes in the bladder, and extravasation of urine. The death was prior to 1885.

In my own experience, at least one death has occurred in a stubborn middle aged man as a result of chronic urethral stricture and the associated secondary infection and uremia. Severe lesions of this kind are much better known in men than in women. If the facts were known, no doubt other women have neglected themselves and died similar deaths secondary to urethral stricture.

The literature on this subject remains rather sparse and only the more recent works were available to the writer. A good discussion of the earlier papers may be obtained in the writings of Stevens, Wynne, Pugh, and Anderson. Suffice it to record here that the Frenchman Lisfranc in 1824 first called attention to the condition of stricture in the female urethra. The first case description was credited to Earl of London in 1828. Then followed papers by Civiale in 1850 and by Newman in 1875. Hermann reviewed the literature on the subject in 1886 and contributed 6 cases of his own to the 23 cases already reported. Vander Werken and Skene published accounts of the disorder in 1887 and the former again in 1890 according to the above authors. In 1892, Otis was observant enough to devise special methods of diagnosis and treatment for slight degrees of stricture.

Kelly and Burnam, in 1914, treated the subject as a rare condition and much of their material was based on the observations of others. They noted however that gonorrhea and obstetrical injuries were the important factors in etiology. Once the stricture had developed, they wrote, cystitis was very apt to follow. Their methods of treatment, aside from dilation of the urethra, seem strange today.

All are agreed that relatively little was accomplished on the subject before 1922, when Stevens published his first paper in California. He concluded that stricture of the urethra was a common ailment in women which responded very well to adequate treatment. He also pointed out that treatment of the lesion was prophylaxis against more important disorders in the upper urinary system. Gonorrhea, he regarded as the prime factor in the cause of the disease.

In 1924, and again in 1927, Pugh wrote two interesting essays on the subject. In the first paper he gave case reports to prove his points, while in 1927 he discussed the subject in a more academic manner. His conclusions were essentially that stricture of the female urethra was a common condition, caused primarily by chronic gonorrhea, producing various urinary symptoms, and best treated (with good results) by dilation of the urethra.

Cheetham, in 1927, presented 3 cases to emphasize the three main factors in etiology; namely, infection, which was generally gonorrheal, and trauma, both obstetrical and operative. He treated his patients by dilation of the urethra.

Wynne, in 1927, discussed the matter of stricture of the female urethra, paying special attention to the anatomy of the urethra, age groups, and the location and size of the strictures. His 47 cases ranged in age from 19 to 70 years. He noted that gonorrhea and obstetrical trauma were about equal in causing strictures or about 20 per cent each, and that senility was a factor in 10 per cent of his cases. He also found several that were secondary to syphilis.

In 1928, Anderson summarized his results with 60 cases. He emphasized the inflammatory origin of 85 per cent, and 10 per cent he regarded as resulting from obstetrical injuries. He concluded that the lesion was common and responded well to dilations of the urethra.

King, in 1931, wrote an interesting article on the subject of stricture of the female urethra reviewing all available literature and reporting 4 cases of his own. His first case was a very remarkable one showing chronic dilation of the bladder with trabeculations. King also observed trabeculations of the bladder in his fourth case with changes of the trigone in both, but tended to minimize secondary pathology in the kidneys resulting from obstruction in the urethra.

More recently, in 1946, Sinclair described 13 cases of stricture, some of which were complicated by pathologic changes above the bladder.

Hinman's classical book on urology gave a résumé of the anatomy and physiology of the female urethra, and in another section he gave a short discussion of stricture; all very concise and to the point.

Lowsley and Kirwin presented the subject adequately in their two volume work on urology, and they believe that the site of the stricture in the female may be very often palpated.

Herman had a good discussion of the subject for a textbook, emphasizing gonorrhea and other infections of the urethra as causes of stricture as well as trauma. He advised dilations of the urethra as treatment.

Everett's treatment of the subject in his gynecological and obstetrical urology deserves special mention. He pointed out the divergent views concerning the occurrence of stricture in the female urethra, based on different concepts as to what constitutes a stricture. His ideas of etiology, symptoms, diagnosis and treatment conformed very much to those of the other authors referred to in this paper. Everett believes that most strictures occur in the distal part of the urethra.

Boyd has emphasized the occurrence of congenital stricture or stenosis of the female urethra which manifested itself in younger people, with location of the lesion at or near the meatus. Stevens also discussed congenital stricture in his paper of 1936. The author has no first hand knowledge of this particular lesion.

It appears that stricture of the female urethra constituted a much more common and more important lesion than many think it to be, and it may be easily overlooked or ignored or confused with something else. Cheetham as well as Stevens believed that 10 per cent to 35 per cent of women with chronic vesical symptoms have stricture of variable degrees of the urethra as the basis for their symptoms. In 1949 Powell and Powell, using caliber 20F as criterion for the diagnosis, in a study of 603 cases of urethral lesion, found 43 per cent due to stricture.

Stricture of the urethra of inflammatory and traumatic origins undoubtedly constitutes the commonest cause of obstruction in the adult female urethra today. Other less common causes of urethral stricture also include such things as peri-urethral abscesses, certain hypertrophic senile changes in the urethra, perhaps caruncles, associated inflammatory or traumatic changes in some cases of urethrovaginal fistula, and other conditions as diverticula, and so on. How commonly chancroidal, syphilitic, and tuberculous lesions caused stricture was difficult to evaluate. The granulomatous venereal lesions of the female genital organs have also been given as a cause of stricture, particularly among Negroes.

Congenital stenosis of the female urethra also occurs. Hypertrophy of glandular tissue at the vesical orifice produced urethral obstruction very much as does an adenomatous prostate gland in men, and the writer has observed one case. While such things as tumors or growths should be classified as urethral obstructions, they belong in a category other than stricture. The results and effects of any type of urethral obstruction, however, remain essentially the same.

The vast majority of the cases reported earlier were undoubtedly due to inflammatory reactions incidental to gonorrheal infection in the urethra. Stevens, Pugh, and Anderson, as well as others, considered gonorrhea the prime etiological factor and this point of view seems logical and correct. In more recent years, however, it seems doubtful if this thesis remains, because of the widespread use of effective chemotherapeutic drugs in the destruction of the gonococcus and other pathologic micro-organisms which may localize in and about the urethra. Gonorrhea has become definitely less frequent during the past few years, but severe gonorrhea remains as a very specific cause of chronic urethritis and associated stricture formation in both sexes. By the same reasoning inflammatory urethral strictures in both sexes should become less common in the future, by the use of very effective drugs.

Very little was recorded about the actual microscopic pathology of the lesions in the urethra for obvious reasons. It was generally accepted, however, in the severe chronic cases of gonorrhea of the urethra wherein there was destruction of epithelium and ulceration and involvement of the submucosa and muscular layers, that, in healing, more or less scarring occurred depending upon many factors. Contraction of the scar tissue and encroachment on the lumen of the urethra resulted in stricture formation with more or less residual chronic urethritis remaining. Foci of chronic infection in the peri-urethral ducts, and in the small urethral glands or in the glandlike recesses and between the folds of the mucosa, constituted, in all probability, factors in the production of the narrowing of the urethral lumen. Any kind of infection in the urethra which produced ulceration could result in the production of stricture, but nonspecific infections of this grade were certainly not common in women today.

Trauma was also an important factor in the production of stricture of the female urethra. The writer refers particularly to obstetrical trauma, either natural or artificially induced by instrumentation at deliveries, as well as the trauma associated with operative procedures on the female genitalia. Severe pressure of the oncoming head against the symphysis pubis contusing or crushing the urethra, or producing ischemia and a resulting small slough, was probably the mechanism involved in cases of normal deliveries with ensuing stricture formation.

The repeated trauma of vigorous coitus has been mentioned as a cause by certain authors. Other types of direct trauma, particularly accidental, to the urethra could also produce stricture.

In most of the cases reported below, it seemed that trauma, either obstetrical or operative, or both, played the main role in initiating the disorder. Secondary infection was present in some, but when it occurred in time relationship with the trauma was, of course, impossible to determine.

Chemical injuries of the urethra resulting in stricture formation have been observed by Anderson. He referred particularly to the overzealous use of concentrated chemicals in the urethra in an effort to cure gonorrhea. The same distressing condition has been observed in men where its occurrence has undoubtedly been more frequent. The writer recalls 1 case years ago in which the urethra and bladder of a woman were almost completely destroyed by the application of phenol.

Some strictures were reported by some as hard and dense while others were reported as soft and delicate and easily destroyed, and that has been my experience as well. It can be assumed on the basis of the long history in the cases of hard or dense stricture that the condition was one of long standing perhaps with recurrent injuries of several deliveries, either spontaneous or with forceps, or following repeated pelvic operations by the vaginal approach, or by repeated or very severe infections perhaps (cases 2, 3, and 4).

Given a urethral injury from any of several causes, the healing process may be complicated with infection, excessive scar formation with contracture, and ultimate stricture. The strictures may be annular or longitudinal, involving relatively long or short portions of the urethral wall, or mostly the meatus. A certain degree of chronic urethritis remains associated with the stricture.

The female urethra is regarded as analogous to the deep or posterior urethra in the male. It has two para-urethral ducts and a variable number of small glands or gland-like recesses in the mucosa and beneath. The epithelium of the distal portion partakes of the squamous variety and as one approaches the bladder the cells become transitional in type and like those of the trigone and bladder. The urethral mucosa forms numerous longitudinal folds. It has submucosal and muscular coats, as well as a poorly developed corpus spongosium between. The urethra ranges in diameter from 8 to 12 mm. with its narrowest portion at the meatus.

Hinman writes that the urethra varies in length from 2.5 to 5 cm. but the average is probably 3.5 to 4 cm. The normal female urethra will easily take 26F instrument and many 28F without difficulty. The normal urethra stretches very easily, and has a gentle curve (Hinman) beneath the symphysis pubis according to all teaching with which the writer is acquainted. In 1937, however, Stevens and Smith, on the basis of x-ray examinations, insisted that the female urethra was straight, and not curved. Their reproduced x-ray films were very convincing. After repeated deliveries the writer believes that the urethra may lose certain of its nulliparous or virginal features.

Narrowing of the urethra to 20F or less, in the opinion of most authors, constituted mild stricture, and these patients should be so treated. Theoretically, if the narrowing were only slight, producing a lumen of 22F or 24F, this would still be a stricture. In the cases reported below the urethra was definitely less than 20F and ranging about 18F and less. In case 1, the writer has no clear idea of the size of the urethra except that it was unusually small. The presence or absence of stricture can be determined very easily by observing resistance to catheterization with a small soft rubber catheter or more properly by the use of a bougie. In the more severe cases a bougie or ordinary catheter (16 or 18F) cannot be passed, and in mild cases one should feel the hang of the bougie on withdrawing it.

Wynne, in 1927, measured the urethra in 33 cases and found several 2 mm. and less in diameter as well as several others of 3–4 mm. Unfortunately, he gave no data concerning the secondary pathologic changes that occurred above the level of the urethra. In location of the stricture he found that the majority were in the anterior third and about the meatus, while a few involved the entire urethra.

The symptomatology of this group of cases varies somewhat, as a rule, between relatively narrow limits. Most of these women complained of burning or discomfort in the urethra and bladder on urination with more or less frequency of urination. The frequency, however, in the milder cases often completely disappeared at night. Urgency of urination and actual pain and tenseness developed in some cases. A very few noted straining at voiding and others slowness to empty the bladder which may amount to slight straining. An occasional patient observed hematuria of variable degree. Retention of urine was definitely a late symptom judging by the literature and personal observations and not very frequently observed. This was probably also true of dribbling and incontenance. Hysterical retention of urine may also occur (case 6).

The severity of the symptoms also very definitely depends upon the stage of the disorder and the type of secondary infection and other conditions which may develop in the bladder or above. Fever may change the clinical picture, and general malaise with headache etc., and pain or aching in the pelvis and about the kidneys may develop. If the vesical symptoms are not appreciated by a proper history and if the physical examination is not carefully made, the illness may be misjudged and the disorder missed and be regarded as something else. The patient's state of nervousness can also be a misleading factor (case 6).

In the fatal case reported below the patient was in uremia at the time of the first observation and it developed steadily in spite of treatment. (Uremia was probably a factor in the fatal case reported by Heinrichsdorff.) Uremia, of course, may be expected in one of either sex with severe chronic urinary obstruction, especially at the vesical orifice or below, wherein both kidneys become involved.

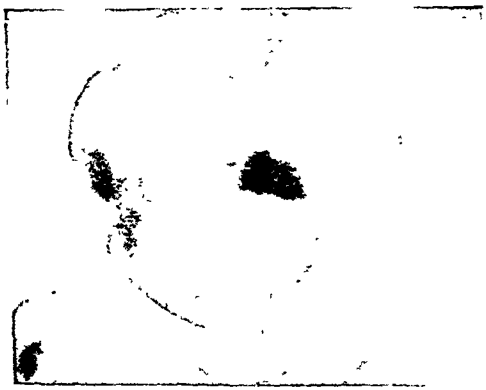

FIG. 1. Case 6. Trabeculated urinary bladder demonstrated by the excretion of intravenous diadrast in 30 minutes.

It was also interesting to note that in some of these patients the illness, often regarded as more or less obscure, often ran a course of years. Chronicity was characteristic of stricture of the female urethra. There were periods of time when the symptoms seemed to clear and this probably can be related to subsiding infection in the bladder and urethra which undoubtedly occurred. When an acute episode of infection developed as it appeared to do, the more acute type of symptoms arose. Among the younger women the symptoms seemed to be of shorter duration because they generally sought professional advice early in the course of their illness.

Physical findings in these cases deserve special consideration. Externally one may observe nothing abnormal and the urethra and anterior vaginal wall may not be unusual in appearance. The presence of thickening along the course of the urethra was impossible to establish in my cases, and there was one with a very dense stricture (case 4). Certain writers however insisted that they could feel the strictured area with the finger in the vagina. Very often these women would complain of discomfort and a desire to void in palpating the base of the urinary bladder or the urethra. It has been my experience, and as found in most of the literature, very little that was positive by physical examination could be found until one passed a catheter or bougie or used other special methods of diagnosis. In some traumatic cases, the meatus may be definitely narrowed or otherwise obscured (cases 2 and 4).

The more marked secondary changes, as dilation of the bladder with retention of urine observed in case 1, have not been described by others except by King. Residual urine of ordinary amounts not comparable to retention of urine, seems likely to have been a feature, but the writer has not observed it nor can references be given.

Muscle spasm and pain in the lower abdomen and in the loins all depended on various degrees of infection in the kidneys and bladder, and back pressure and the like in the late cases. Uremia also occurred in the advanced and neglected cases (case 1).

The urine presented variable findings. In some of the milder cases the catheterized urine showed relatively little that was unusual and this point has been mentioned by Cheetham and Everett. In most of the moderately severe cases however, the urine gave evidence of infection such as turbidity, traces of albumin and variable numbers of cells, leukocytes, mostly; but then at times erythrocytes may have been present. In these urines, bacteria of one sort or another were generally found. The writer believes that the character of the urine may change as an episode of acute infection subsides or clears up, as in the milder cases, especially following treatment with one of the more effective chemotherapeutic drugs. The histories in some of the mild cases also indicated perhaps that the infection may have cleared up at times without treatment, but it may have again recurred when local conditions changed. In cases of severe obstruction with residual urine, medication to destroy infection was of no avail until the obstruction was relieved and this stands as an important principle in treatment.

Cystoscopically, interesting conditions may be observed. The vesical orifice was found negative in the few cases examined by the writer but the trigone was almost always hyperemic with occasional hemorrhagic points and sometimes edematous. In cases 3, 4, and 6 the bladder presented trabeculations indicating hypertrophy from overwork in expelling the urine against the resistance of the stricture. Similar findings were recorded by those authors who took the trouble to pass a cystoscope, particularly Sinclair and King. Evidence of various degrees of cystitis has been found which was the origin of the hematuria.

The urethra has been examined by some with suitable instruments and whitish scars at the sites of the stricture have been described (case 6).

Of course, other mild to marked secondary changes become obvious and may occur in the upper urinary system if the lesion is of long standing and severe enough. Some of these features were observed by Sinclair and published in 1926, King in 1931, and others, and by the author. Determination of renal function, urography, bacteriological studies, blood chemistry, etc., were all obvious enough, necessary, and indicated to complete the case study.

There was general agreement in the treatment of these cases, which consisted primarily of graded dilations of the urethra and measures aimed at clearing up the active infection in the urinary system, which was generally in the bladder. Dilation in the severe and dense strictures must be made under anesthesia of one kind or another—especialy caudal or pentothal. In the milder cases the author has simply drained the bladder and inserted 20–25 cc of 3 per cent solution of butyn as preparation for dilations. The dilations must, of course, be repeated at fairly frequent intervals in most cases, while in the more severe cases the treatments may be performed every third or fourth day for a longer period. Dilations must be kept up until all signs of stricture and the associated urethritis disappear and they may drag out over a considerable period of time in some cases. Recurrences are to be expected especially in the cases of severe strictures, and if treatment has been inadequate.

Irrigations of the bladder with warm boracic or permanganate or other solutions also gave relief and helped to clear up the cystitis. The use of chemotherapeutic drugs, as indicated, also stood as considerable aid, and these measures were very important. A large intake of fluids was an essential part of the treatment in those cases, particularly, with active infection.

It has been the experience of the author that the ordinary case of urethral stricture in women responded readily to treatment and if care was exercised in relieving pain, the patients would cooperate.

At this point the writer wishes to emphasize that it does no harm, and perhaps much good, to pass urethral sounds in those women with apparently simple cystitis or urethritis as they clear up, because of the possibility of stricture. By clearing up the nidus of the infection in the urethra, the vesical infection will probably not recur. Cystitis can seldom be regarded as a primary disease.

Urethral sounds for use in the female urethra are urgently needed. Insofar as the author is aware, there are no sounds made for the female urethra. One must depend upon Hager uterine dilators or the sounds for men with their marked curve. A set of sounds from 8F to 28F for use in women and children seems very essential indeed, yet the writer has not been able up to this time to interest any manufacturer of instruments in this project. If the female urethra is essentially straight and not curved as we formerly thought, the use of the sounds for the male urethra can do harm or at least produce more pain during treatment than may be justified.

The sounds should be not more than 16 cm. in length and with only the slightest curve.

ABSTRACTS OF CASES

Case 1. Mrs. S. C., aged 51, July 1948. Diagnosis: Severe stricture of the urethra with chronic retention of urine; acute and chronic anemia; uremia and death. Vesical symptoms for a long period of time. During the past few weeks the patient had marked difficulty in voiding, with frequency and passing only small amounts of urine and with constant desire to void. She had been drowsy for many days. She had also lost considerable weight and strength during the year. The patient was a nurse 25 years ago. She was the mother of two children, but details of deliveries were not obtained.

Examination showed an extremely emaciated weak and listless white woman who was also pale and dehydrated. Temperature 100F, pulse 110, blood pressure 120/40. The abdomen presented dilation of the urinary bladder which almost reached the umbilicus. Pelvic examination was negative. Catheterization was performed with 14F catheter after the nurse had failed in the first attempt. The urine was pale and turbid, showing albumin and staphylococci.

Urethral dilations were performed with 14, 16, 18 and 20F sounds and a Foley retention catheter was inserted. The bladder was gradually decompressed.

Blood: Red blood cells 3,370,000; white blood cells 14,100, hemoglobin 60 per cent. Nonprotein nitrogen 120 mg., uric acid 7.6 mg., creatinine 6.25 mg.

The patient did not respond well to treatment consisting essentially of 4 liters of fluids daily, two blood transfusions early in the course of hospitalization, catheter drainage of the bladder and irrigations of the same, as well as penicillin in large doses and general measures. At no time did her daily blood pressure exceed 130 systolic. Phenolsulfonphthalein excretion was zero in 4 hours. She ran a febrile course and was typically uremic during the most of the 14 days in the hospital. She died of uremia and sepsis with associated terminal acidosis (CO_2 21 per cent, nonprotein nitrogen 129).

It is difficult to conceive of a properly trained nurse as this patient and her husband insisted that she was, allowing herself to get into such a deplorable state. The diagnosis of stricture of the urethra was very clear and the several irreversible secondary pathologic changes, sufficient to cause death followed as a result of the severe and long standing chronic obstruction in the urethra. We have no idea as to the underlying cause of the stricture in this case.

Case 2. Mrs. B. B., aged 27, June 1930. Diagnosis: Stricture of the urethra and chronic cystitis. Six years before examination the patient first noted painless hematuria associated with frequency of urination. The hematuria recurred once just before she came under observations. In the interval she had had various episodes of vesical symptoms.

She had been pregnant 5 times, two of which terminated prematurely and were followed by curettements.

Examination revealed a poorly nourished white woman, whose urethral meatus appeared small. Other details of the examination were negative. Catheterization was performed with difficulty using a 18F catheter. The urine was infected and contained albumin. Phenolsulfonphthalein excretion was 60 per cent in 2 hours. Cystoscopy under caudal anesthesia revealed the presence of a fairly dense urethral stricture just inside the meatus. The urethra was dilated to 24F before the cystoscope could be passed. The bladder revealed slight edema and injection of the trigone only.

The urethra was dilated several times at 5 to 10 day intervals reaching 26 and 28F as the treatment progressed. All symptoms disappeared and the urine cleared up. Permanganate irrigations of the bladder followed each of the dilations. Her general condition improved during the 3 years she was under observation. No recurrences of the urethral disorders observed.

This is a rather typical case of stricture of the distal part of the urethra in a multipara. We have no clear indication of the etiology of the stricture, but the possibility of trauma on the urethra from the three full term deliveries, and that perhaps from the curettements, may have caused the stricture.

Case 3. Mrs. A. F., aged 58. September 1948. Diagnosis: Stricture of the urethra and associated recurrent cystitis and acute pyelonephritis; chronic anemia and poor nutrition. The patient had been acutely ill several days before admission to the hospital with pain and discomfort in the bladder and urethra, frequency of urination with urgency and burning, as well as chills and fever. She also stated that she had had similar but less severe episodes as far back as 20 years. Generally the attacks cleared or almost cleared without medication in a few days or couple of weeks. She had been pregnant 5 times, two of which terminated normally, while three ended in abortions or miscarriage. She had been curetted following each of the three imperfect pregnancies.

Examination revealed a poorly nourished, acutely ill and anemic patient with temperature of 102F. There was pain about the left kidney. Catheterization with small catheter was performed by the nurse; no difficulty recorded. The urine showed albumin and pus.

The acute infection was treated by a large fluid intake and penicillin and it subsided in a few days. Nonprotein nitrogen 28 mg. Red blood cells 3,560,000; white blood cells 5,600; hemoglobin 70.

An excretory urogram was negative.

Cystoscopy was performed when she was afebrile. An unsuspected stricture of the urethra was found, moderate in extent and fairly dense, involving the central part of the urethra. Bleeding occurred following the passage of the cystoscope as well as the occurrence of pain locally. The bladder was slightly hyperemic and slightly trabeculated.

One blood transfusion was given. The patient was treated by urethral dilations on several occasions up to 28F. All vesical symptoms disappeared and she voided a normal stream of urine. The patient's general condition improved.

The patient probably sustained an injury or injuries to her urethra as a result of the three curettements of the uterus. Secondary infections in the bladder then occurred and cleared up it seems, to recur again and again. She probably had acute left pyelonephritis at the time of admission to the hospital, all secondary to obstruction in the urethra.

Case 4. Mrs. S. M., aged 54. March 19, 1949. Diagnosis: Stricture of the urethra, chronic recurrent cystitis and operative scarring of the perineum and vagina. Some weeks before observation the patient noticed considerable hematuria, smarting and burning on urination. The bleeding ceased, but the other symptoms persisted. She also had to strain a little to void. She had had previous episodes of vesical symptoms but never hematuria. The first episode of difficulties with the bladder occurred 7 to 8 years ago and about 2 years following perineal and vaginal operations. Six full term pregnancies had occurred.

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Examination showed considerable scarring in the posterior vaginal wall and perineum and less so in the anterior vaginal wall. The vagina was narrow and scarred. The urethral meatus appeared to be small. An excretory urogram was negative. Catheterization by the nurse using a 14 or 16F catheter revealed clear and uninfected urine. A cystoscope could not be passed until the urethra was dilated, which caused pain and slight bleeding. The dense stricture was located in the central part of the urethra as well as at the meatus. The bladder showed hyperemia of the trigone with evidence of tiny hemorrhages as well as trabeculations.

The patient had her urethra dilated under butyn anesthesia at weekly intervals for 6 weeks. The sounds were gradually worked up to 26 and 28F. The patient experienced great relief and voided a full stream without difficulties. No recurrences have been recorded to this date.

It seems to the writer that we have a fairly clear case of stricture of the urethra directly related to probable trauma and infection of a perineal and vaginal operation. There may also have been an obstetrical injury but we have no conclusive evidence. The hematuria was probably secondary to the recurrent cystitis.

Case 5. Mrs. D. K. H., aged 25, February–March 1950. Diagnosis: Stricture of the urethra. Bladder irritation, recurrent in nature, had troubled the patient for 2 years, beginning shortly after her marriage. The cystitis had been treated with sulfa drugs, but recurrences developed 8 to 10 times in the 2 year period lasting a few days to two weeks an episode. The symptoms were mainly frequency and burning.

Examination showed a healthy young white woman. Pelvic and abdominal examination were negative. Catheterization was performed with an 18F catheter and the same size bougie was the only one that would pass, definitely demonstrating a stricture. Urine was uninfected and clear.

Treatment consisted of graded dilations of the urethra on 7 different occasions under butyn anesthesia. The first time a 24F sound was passed a very little blood appeared at the meatus. Her symptoms disappeared after the third or fourth treatment and she has been well since, voiding a full stream of urine.

A simple case of stricture of the urethra showing as one of cystitis which had often cleared up with chemotherapy only to recur again and again. The underlying cause of the stricture was not apparent. (The writer has records of other similar mild cases.)

Case 6. Mrs. K. E. C., aged 40, an hysterical white woman with stricture of the urethra, whose history was too complicated to record. She had been treated for recurrent cystitis elsewhere and the stricture was overlooked. One of the remarkable features about the case was the extent of trabeculations of the bladder from urethral obstruction, as shown in the excretory urogram (fig. 1) and at cystoscopy. She also exhibited whitish scarring in the urethra at the site of the stricture when examined with the panendoscope. The vesical orifice was normal.

CONCLUSIONS

Stricture of the female urethra must be regarded as common and important but often an unrecognized lesion in those with vesical and urethral symptoms.

There are two main causes of stricture of the female urethra today: first, traumatic arising from obstetrical and surgical injuries to the urethra, and second, inflammatory following gonorrheal urethritis.

Adequate treatment, particularly graded dilations, gives good results.

In long standing cases of urinary obstruction due to stricture of the urethra, mild to marked secondary pathologic changes develop in the urinary system.

Death has occurred from sepsis and uremia arising secondarily from such a seemingly slight lesion as stricture of the female urethra.

The third case of death incidental to stricture of the urethra in the female is reported.

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REFERENCES

Anderson, A. E.: Northwest. Med., 27: 520, 1928.
Boyd, M. L.: J. A. M. A., 92: 2154, 1929.
Cheetham, J. G.: Northwest. Med., 26: 539, 1927.
Everett, H. S.: Gynecological and Obstetrical Urology. Baltimore: Williams and Wilkins, 1947.
Heinrichsdorff: Zentralbl. f. Gynak. 44: 1081, 1920. (Abstract prepared by W. F. Prior Co. Hagerstown, Md.)
Hinman, F.: Principles and Practices of Urology. Philadelphia: W. B. Saunders Co., 1935.
Herman, L., Practice of Urology. Philadelphia: W. B. Saunders Co. 1938.
King, M. W. Am. J. Surg., 13: 251, 1931.
Kelly, H. A. and Burnham, C. F.: Diseases of the Kidneys, Ureters and Bladder. New York: Appleton, 1914.
Lowsley, O. S. and Kirwin, T. J.: Clinical Urology. Baltimore: William and Wilkins, 1944.
Powell, N. B. and Powell, E. B.: J. Urol., 61: 557, 1949.
Pugh, W. S.: Ann. Surg., 79: 770, 1924.
Pugh, W. S.: J. A. M. A., 87: 1790, 1926.
Sinclair, D. A.: Urol. & Cut. Rev., 50: 389, 1946.
Stevens, W. E.: Calif. St. J. Med., 20: 51, 1922.
Stevens, W. E. J. A. M. A., 106: 89, 1936.
Stevens, W. E. and Smith, S. P.: J. Urol., 37: 194, 1937.
Wynne, H. M. N.: Surg. Gynec. & Obst., 34: 208, 1927.

Examination showed considerable scarring in the posterior vaginal wall and perineum and less so in the anterior vaginal wall. The vagina was narrow and scarred. The urethral meatus appeared to be small. An excretory urogram was negative. Catheterization by the nurse using a 14 or 16F catheter revealed clear and uninfected urine. A cystoscope could not be passed until the urethra was dilated, which caused pain and slight bleeding. The dense stricture was located in the central part of the urethra as well as at the meatus. The bladder showed hyperemia of the trigone with evidence of tiny hemorrhages as well as trabeculations.

The patient had her urethra dilated under butyn anesthesia at weekly intervals for 6 weeks. The sounds were gradually worked up to 26 and 28F. The patient experienced great relief and voided a full stream without difficulties. No recurrences have been recorded to this date.

It seems to the writer that we have a fairly clear case of stricture of the urethra directly related to probable trauma and infection of a perineal and vaginal operation. There may also have been an obstetrical injury but we have no conclusive evidence. The hematuria was probably secondary to the recurrent cystitis.

Case 5. Mrs. D. K. H., aged 25, February–March 1950. Diagnosis: Stricture of the urethra. Bladder irritation, recurrent in nature, had troubled the patient for 2 years, beginning shortly after her marriage. The cystitis had been treated with sulfa drugs, but recurrences developed 8 to 10 times in the 2 year period lasting a few days to two weeks an episode. The symptoms were mainly frequency and burning.

Examination showed a healthy young white woman. Pelvic and abdominal examination were negative. Catheterization was performed with an 18F catheter and the same size bougie was the only one that would pass, definitely demonstrating a stricture. Urine was uninfected and clear.

Treatment consisted of graded dilations of the urethra on 7 different occasions under butyn anesthesia. The first time a 24F sound was passed a very little blood appeared at the meatus. Her symptoms disappeared after the third or fourth treatment and she has been well since, voiding a full stream of urine.

A simple case of stricture of the urethra showing as one of cystitis which had often cleared up with chemotherapy only to recur again and again. The underlying cause of the stricture was not apparent. (The writer has records of other similar mild cases.)

Case 6. Mrs. K. E. C., aged 40, an hysterical white woman with stricture of the urethra, whose history was too complicated to record. She had been treated for recurrent cystitis elsewhere and the stricture was overlooked. One of the remarkable features about the case was the extent of trabeculations of the bladder from urethral obstruction, as shown in the excretory urogram (fig. 1) and at cystoscopy. She also exhibited whitish scarring in the urethra at the site however, this is a common finding in metropolitan districts. There was no evidence of tuberculous disease of the epididymides, vasa deferentia, or seminal vesicles. The usual careful examination of the abdomen failed to reveal any tenderness or enlargement of the kidneys. Routine examination of the urine of these patients did not indicate the presence of tuberculosis anywhere in the urinary tract. Blood chemistry and renal function tests were normal in all instances before surgery was performed. The hemograms were not unusual.

CASE REPORTS

Case 1. I. S., a 79 year old man, was admitted to the hospital January 2, 1940, and was discharged January 25, 1940. He had had nocturia 4 to 6 times, urgency, hesitancy, and burning for 3 months. Rectal examination revealed slight enlargement of the prostate gland. It was smooth in contour and of normal consistency. There was no residual urine. Cystoscopic examination showed a grade 1 enlargement of the middle and lateral prostatic lobes. Blood chemistry, blood counts, and renal function tests were all normal. The urine contained 50–60 pus cells, 20 to 30 red cells, and many bacteria per high power microscopic field. The diagnosis was benign prostatic hypertrophy. Five grams of tissue were resected on January 8, 1940. The highest temperature was 103F on the third postoperative day. Convalescence was uneventful and the patient was discharged from the hospital on the seventeenth postoperative day. He received routine care at an old people's home. Minimal dysuria and nocturia one time persisted during the ensuing few months. Histologic examination revealed chronic tuberculosis of the prostate gland.

Case 2. J. D., a 65 year old man, was admitted to the hospital on November 19, 1944, and was discharged June 14, 1945. He was admitted for observation of reputed tuberculosis of the spine. He was seen in urological consultation on January 18, 1945. He gave a history of many prostatic massages and urethral instillations for prostate gland infection. Rectal examination revealed a small, sclerotic prostate gland. Four ounces of residual urine were found. Cystoscopic examination revealed a grade 2 fibrous bar associated with dilated prostatic duct orifices. Blood chemistry, blood counts, and repeated urinalysis were within normal limits. The diagnosis was fibrous bar. Two grams of fibrous tissue were resected on February 15, 1945. The temperature, recorded at 103F on the second day, became normal on the fifth postoperative day. A smooth convalescence was noted during his prolonged hospitalization. The urine contained a few pus cells but urine cultures were negative. He had no unusual frequency, nocturia, or dysuria. The resected tissue was reported as marked chronic tuberculous inflammation of the prostate gland. See figure 1, *A*.

Case 3. P. L., a man 75 years of age, was admitted to the hospital September 11, 1945, and was discharged October 30, 1945. He complained of frequency, hesitancy, and nocturia of only 3 weeks' duration. A grade 2 enlargement of the prostate gland was noted. The left lobe was hard on palpation; the right lobe was moderately hard. No residual urine was found. Cystoscopic examination revealed a grade 2 commissural bar and lateral prostatic lobe hypertrophy. Blood chemis-

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TUBERCULOSIS IN THE OBSTRUCTIVE PROSTATE GLAND

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Examination of surgically removed prostate glands during the past 10 years has revealed tuberculous infection in 11 instances. Pertinent information concerning the clinical course of these patients will be discussed.

Tuberculosis of the prostate gland is not an unusual entity since the prostate gland is involved in about 75 per cent of all urogenital tuberculosis. Surgery on the tuberculous prostate gland has been contraindicated because the danger of disseminating the tuberculosis is real. Serious complications such as lack of healing, persistent fistula formation, and spontaneous sloughing into the urethra, the bladder, the rectum, the perineum, and even the peritoneum dictate the conservative management.

Reports of tuberculosis in surgically removed prostatic tissues have become commonplace in the urological literature. The incidence of any complication has been minimal and the operative results have been excellent. The tuberculous lesions were not diagnosed preoperatively but they were found on careful examination of the tissues by the pathologist.

McDonald has stressed the importance of recognizing granulomatous prostatitis which may be interpreted as tuberculous prostatitis. A diagnosis of tuberculosis cannot be made by histological examination alone. The presence of tuberculosis must be proven on bacteriological studies. However, the first intimation of tuberculosis follows histological examination of the prostatic tissues at which time the tissues have been fixed and are unsatisfactory for guinea pig inoculation or cultural studies.

Tuberculous infection has been diagnosed by the pathologist on tissue analysis of each of the following surgical specimens. The following remarks do not apply in proving or disproving that tuberculosis is limited to the prostate gland. We are interested in the clinical course of patients whose surgical specimens have revealed tuberculosis on histopathological study. We do not claim to have made exhaustive studies to rule out other foci of tuberculosis, but none were apparent either pre- or postoperatively. All patients had symptoms of bladder neck obstruction, and operation was done for removal of the obstruction. Perineal biopsies were indicated in 2 patients because nodules, suspicious of early carcinoma, were present.

In reviewing the records of 11 patients with tuberculosis of the prostate gland, certain details were noteworthy. Only one patient had any evidence of active tuberculosis; he was admitted to the hospital with Pott's disease. None of the others had any obvious tuberculous lesion nor did they give a personal history of tuberculous infection.

Most of the patients had healed pulmonary lesions on x-ray examination;

tient clinic was essentially normal. His only persistent symptom was nocturia. The tissue was reported as casous tuberculosis of the prostate gland.

Case 4. M. C., a man 49 years of age, was admitted to the hospital December 22, 1945, and was discharged January 6, 1946. He had had suprapubic and urethral pain for one month before admission to the hospital. The pain had been associated with frequency and nocturia. Rectal examination revealed a grade 2 symmetrical enlargement of the prostate gland. One small nodule was palpated in the midline. There was no residual urine. Roentgen study revealed calcification in the region of the prostate gland. Cystoscopy revealed a grade 1 lateral lobe prostatic hypertrophy. Blood chemistry and blood counts were normal. A few pus cells were found in the urine. The diagnosis was benign prostatic hypertrophy associated with calculus of the prostate gland. Fifteen grams of prostate gland tissue were resected on December 24, 1945. The temperature persisted between 101 and 103F during the first 7 days after which the temperature gradient continued toward normal. He was discharged on the thirteenth postoperative day. His course was marked by an acute left epididymitis on the twentieth postoperative day which responded without incident to the usual therapy. An anterior urethral stricture also responded to repeated, careful urethral dilatations. Histologic examination of the resected tissue revealed chronic tuberculous inflammation of the prostate gland. See figure 1, *B*.

Case 5. C. C., a man 48 years old, was admitted to the hospital on October 28, 1939, and was discharged October 29, 1939. He had been seen at intervals for treatment of a low grade, nonspecific infection of the prostate gland. He was admitted to the hospital for biopsy of an indurated area in the left lateral lobe of the prostate gland. The biopsy, taken with a biopsy punch forceps, was reported as chronic tuberculosis of the prostate gland. Tuberculin treatment was given and the nodule gradually resolved. A transurethral resection was performed on October 29, 1947. Twelve grams of tissue were resected. The tissue was reported as glandular hyperplasia of the prostate gland. The postoperative course was uneventful. The urine has remained normal. The patient presents himself for rectal examination every 6 months. The prostatic capsule and adnexa have remained normal.

Case 6. J. A., a man 59 years old, was admitted to the hospital November 20, 1947, and was discharged December 5, 1947. He had received office treatment for chronic nonspecific prostatitis. He was admitted to the hospital for biopsy of a nodule in the right lobe of the prostate gland which was suspicious of early carcinoma. Blood counts and blood chemistry were normal. The urine contained a few pus cells. On November 21, 1947, a frozen section biopsy, obtained by perineal exposure, was reported as inflammatory tissue. A simple perineal prostatectomy was then performed. The removed prostate gland weighed 10 gm. No remarkable rise in temperature occurred, and the wound healed per primam. The biopsy and prostate gland were subsequently reported as chronic tuberculosis of the prostate gland. See figure 1, *C*. A five day course of streptomycin was given. The patient was discharged from the hospital on try, blood counts, and urine examination were normal. The blood serum acid phosphatase determination was 0.6 Bodansky units. The diagnosis was carcinoma of the prostate gland. Transurethral resection was performed on October 13, 1945. There was no remarkable postoperative rise in temperature. The patient voided well, he had no residual urine, and the nocturia had decreased on discharge on the seventeenth postoperative day. Urine examination in the out-pa-

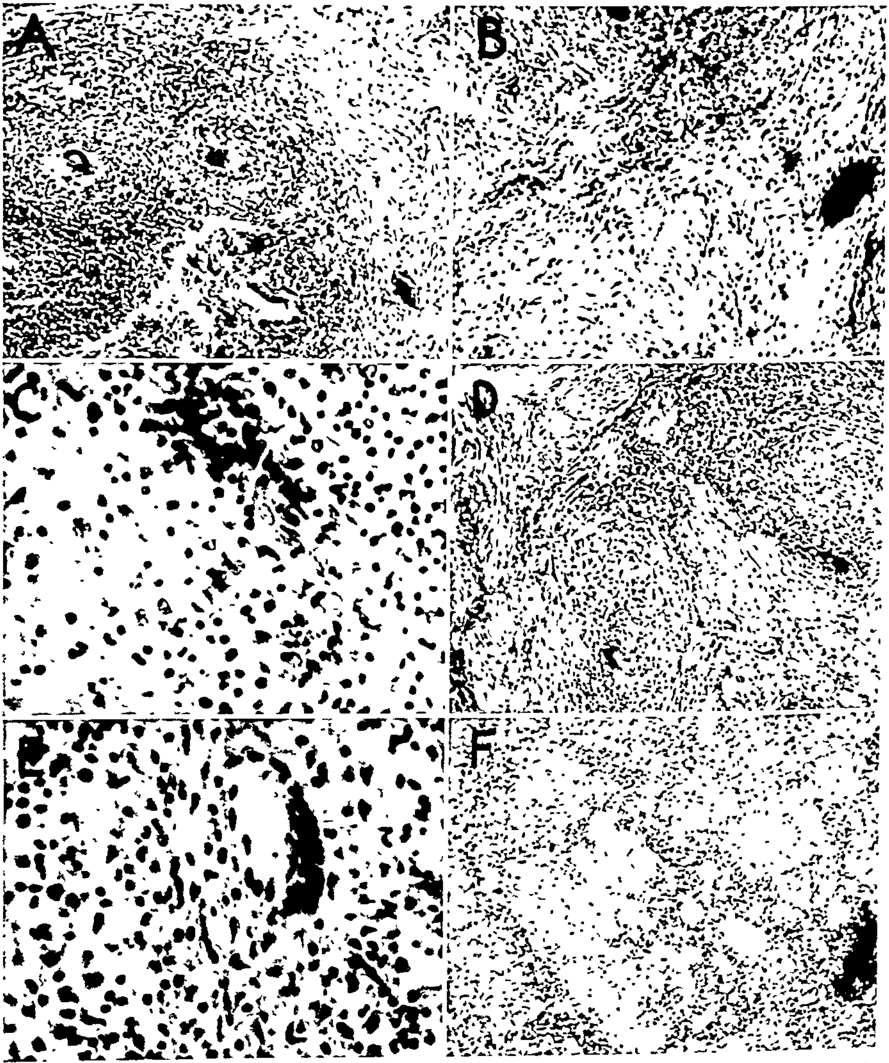

FIG. 1. *A*, chronic tuberculous inflammation of prostate gland removed by transurethral resection. *B*, chronic tuberculous inflammation of the prostate gland removed by transurethral resection. *C*, chronic tuberculosis of prostate gland removed by perineal prostatectomy. *D*, chronic tuberculosis of prostate gland removed by transurethral resection. *E*, chronic tuberculosis of prostate gland removed by transurethral resection. *F*, chronic caseous tuberculosis of prostate gland removed by suprapubic enucleation.

patient recovered his strength and had no urinary symptoms. The pathological study revealed marked glandular hyperplasia and chronic caseous tuberculosis of the prostate gland. See figure 1, *F*.

Case 10. J. G., a man aged 54, was admitted to the hospital on September 14, 1943, and was discharged October 1, 1943. He gave a history of nocturia every hour and hesitancy of 2 weeks' duration. The prostate gland was slightly enlarged on rectal examination. The right lobe was larger and firmer than the left lobe. No residual urine was found. Cystoscopy revealed a small commissural bar and low grade hypertrophy of the lateral prostatic lobes. Blood counts, blood chemistry, and urinalysis were normal. The diagnosis was benign prostatic hypertrophy. Four grams of obstructing tissue were resected on September 22, 1943. The postoperative course was uneventful, and the patient was discharged on the ninth postoperative day. He had no unusual complaints when seen in the out-patient clinic. Histologic examination of the resected tissue showed tuberculous prostatitis with chronic nonspecific infection.

Case 11. B. C., a man 71 years of age, was admitted to the hospital on January 5, 1947, and was discharged February 8, 1947. He had symptoms for only 1 month. During this interval he had nocturia 5 times, a small stream and incontinence. The bladder was found to be distended to the umbilicus. The prostate gland was enlarged grade 1½. The gland seemed fixed and contained a nodule 2 cm. in diameter in the left lobe. The bladder was decompressed slowly, and the patient was given supportive therapy. Before surgery the blood chemistry, blood counts, and urinalysis were normal. Blood serum acid and alkaline phosphatase determinations were within normal limits. The diagnosis was carcinoma of the prostate gland. On January 8, 1947, 13 gm. tissue were resected. Eight grams were removed at a second resection on January 29, 1947, because of excessive amounts of residual urine. The postoperative course was marked by minimal reaction. The patient was discharged on the tenth postoperative day. He had 1 ounce of residual urine. Both surgical specimens were reported as tuberculous prostatitis associated with hyperplasia of the prostate gland. Routine postoperative care was given in the out-patient clinic. Nocturia one time was his only persistent symptom.

DISCUSSION

The salient features in the case reports of these patients have been assembled. Reference to the tables makes a few generalizations possible.

The age distribution of these patients is comparable to any series of bladder neck obstructions although 4 of the 11 were under 50 years of age, which seems to be a rather high percentage (table 1).

Six of the 11 patients volunteered that their symptoms were less than 6 months in duration. This brief interval seemed significant. Also remarkable was the fact that most of these patients had irritable bladders and operation was performed to relieve the symptoms. The amount of residual urine was marked in 2 patients only. One of the latter was admitted in acute retention and the other had the paradoxical incontinence of an overflow bladder.

the fourteenth postoperative day, but he complained of severe bladder irritability. Three weeks postoperatively, acute right epididymitis developed and responded without incident to the usual therapy. Scarring in the posterior urethra has been controlled with dilatations. At present, the patient is remarkably improved but minimal dysuria persists.

Case 7. A. R., a man 45 years of age, was admitted to the hospital on February 15, 1948, and was discharged February 25, 1948. He gave a history of frequency, urgency, and a small stream for 1 year. The prostate gland was enlarged grade 1½. There were no nodules or fixation. A firm area in the right base of the prostate gland was tender on palpation. Four ounces of residual urine were found on catheterization. The obstruction was found to be a glandular bar. Blood chemistry, blood counts, and urinalysis were normal. Four and one-half grams of obstructing tissue were resected on February 18, 1948. There was no rise in temperature. He was discharged on the seventh postoperative day. His immediate course was uneventful. The patient was seen in the office one and two months postoperatively. He had no complaints. No residual urine was present, and the urine was essentially normal. The pathological report was glandular hyperplasia and chronic tuberculosis of the prostate gland. See figure 1, *D*.

Case 8. L. C., a man 65 years of age, was admitted to the hospital April 19, 1948, and was discharged May 2, 1948. He had nocturia, dysuria, and urgency of 6 months' duration. Rectal examination revealed that the prostate gland was enlarged grade 1. It was symmetrical and no nodules or fixation were noted. There was no residual urine. Cystoscopy revealed a posterior commissure and lateral prostatic lobes, grade 1. Blood chemistry, blood counts, and urinalysis were normal. The diagnosis was benign prostatic hypertrophy. On April 21, 1948, 8 gm. of tissue were resected. Streptomycin therapy was started on the third postoperative day when the temperature was recorded at 105F. The temperature gradient reached normal on the eighth postoperative day. Otherwise the postoperative course was not unusual and the early and late results were excellent. He was discharged on the twelfth postoperative day. This patient was seen in May 1950. At this time he mentioned that nocturia one time persisted. The resected tissue was reported as chronic tuberculosis and glandular hyperplasia of the prostate gland. See figure 1, *E*.

Case 9. C. S., a man 74 years of age, was admitted to the hospital on March 3, 1948, and was discharged April 7, 1948. He was hospitalized because he had acute urinary retention of 24 hours' duration. He had had symptoms of bladder neck obstruction for 5 or 6 years. The prostate gland was enlarged grade 4 and was benign on palpation. Blood chemistry and blood counts were normal. Ten to fifteen red cells per high power microscopic field were due to repeated catheterizations. The diagnosis was benign prostatic hypertrophy. On March 9, 1948, a primary suprapubic prostatectomy was performed. The prostate gland weighed 150 gm. The temperature remained elevated for 6 days, but it fell to normal 48 hours after instituting streptomycin therapy. The wound was dry on the fourteenth postoperative day, and the patient voided well. Subsequent care was administered by the patient's home town physician. He reported that the patient recovered his strength and had no urinary symptoms. The pathological study revealed marked glandular hyperplasia and chronic caseous tuberculosis of the prostate gland. See figure 1, *F*.

Case 10. J. G., a man aged 54, was admitted to the hospital on September 14, 1943, and was discharged October 1, 1943. He gave a history of nocturia every hour and hesitancy of 2 weeks' duration. The prostate gland was slightly enlarged on rectal examination. The right lobe was larger and firmer than the left lobe. No residual urine was found. Cystoscopy revealed a small commissural bar and low grade hypertrophy of the lateral prostatic lobes. Blood counts, blood chemistry, and urinalysis were normal. The diagnosis was benign prostatic hypertrophy. Four grams of obstructing tissue were resected on September 22, 1943. The postoperative course was uneventful, and the patient was discharged on the ninth postoperative day. He had no unusual complaints when seen in the out-patient clinic. Histologic examination of the resected tissue showed tuberculous prostatitis with chronic nonspecific infection.

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TABLE 1

	NAME	AGE	SYMPTOMS	DURATION	RESIDUAL
1.	I. S.	79	Nocturia, urgency, burning	3 mos.	0
2.	J. D.	65	Nocturia, dysuria	Years	120 cc
3.	P. L.	44	Nocturia, hesitancy	3 wks.	0
4.	M. C.	49	Nocturia, frequency	1 mo.	0
5.	C. C.	48	Backache, perineal discomfort	Years	0
6.	J. A.	59	Perineal discomfort, strictures	Years	0
7.	A. R.	45	Poor stream, urgency, frequency	1 yr.	120 cc
8.	L. C.	65	Nocturia, urgency, dysuria	6 mos.	0
9.	C. S.	74	Acute retention, urgency	6 yrs.	—
10.	J. G.	54	Nocturia, hesitancy	2 wks.	0
11.	B. C.	71	Poor stream, nocturia, dribbling	1 mo.	Overflow

TABLE 2

	RECTAL FINDINGS	CYSTOSCOPIC FINDINGS	DIAGNOSIS
1.	Slight enlargement—benign	Median lobe	B.P.H.
2.	Small and sclerotic	Grade 2 bar	Bar
3.	Grade 2, hard left lobe	Commissure and laterals	Ca.
4.	Grade 2, nodule in midline	Grade 1 laterals	Calculus
5.	Nodule in left lobe	Commissure	Ca.
6.	Nodule in right lobe	None	Ca.
7.	Firm and tender right base	Commissure	B.P.H.
8.	Grade 1, benign	Commissure	B.P.H.
9.	Grade 4, benign	None	B.P.H.
10.	Right lobe large and firm	Commissure and laterals	B.P.H.
11.	Nodule in left lobe	Commissure and laterals	Ca.

TABLE 3

	SURGICAL PROCEDURE	GRAMS	PATHOLOGY
1.	T.U.R.	5	Chronic tuberculous inflammation
2.	T.U.R.	2	Chronic tuberculous inflammation
3.	T.U.R.	?	Caseous tuberculosis and glandular hyperplasia
4.	T.U.R.	15	Caseous tuberculosis and glandular hyperplasia
5.	Perineal biopsy*	12	Chronic tuberculous inflammation
6.	Perineal biopsy**	40	Chronic tuberculosis and glandular hyperplasia
7.	T.U.R.	4.5	Chronic tuberculosis and glandular hyperplasia
8.	T.U.R.	8	Chronic tuberculosis and glandular hyperplasia
9.	S.P. enucleation	150	Caseous tuberculosis and glandular hyperplasia
10.	T.U.R.	4	Chronic tuberculous inflammation
11.	T.U.R.	21	Chronic tuberculosis and glandular hyperplasia

* T.U.R.

** Perineal prostatectomy.

A high incidence of asymmetry of the prostate gland was detected on rectal examination and ranged from the fibrous induration of chronic infection to the stony hardness of carcinoma or calculous disease. Carcinoma was diagnosed in

4 of the 11 patients although there was no elevation of either acid or alkaline phosphatase. Perineal biopsies were indicated in 2 of the 4 because the nodules were small, and radical perineal prostatectomy was considered for each of them. Both biopsies were reported as tuberculosis of the prostate gland (table 2).

Cystoscopic findings were not suggestive of tuberculous infection.

The surgical procedures used and the amounts of tissue removed are listed in table 3. Glandular hyperplasia was associated with the tuberculosis in 7 instances. Nonspecific prostatitis with contracture of the vesical neck was the dominant associated lesion in the other 4 patients.

We did not recognize delayed healing or prolonged convalescence or any other unusual feature in the postoperative courses (table 4). The care of the surgical patients has been routine and the results are comparable with those secured with surgery on the benign prostate gland.

TABLE 4

	COURSE		COMPLICATIONS	P.O. DAYS
	Immediate	Late		
1.	Febrile 10 days		None	17
2.	Normal		None	14
3.	Normal	Nocturia 4–5	None	17
4.	Febrile 7 days	Stricture urethra	Epididymitis	13
5.	Normal		None	8
6.	Primary healing	Stricture urethra	Epididymitis	14
7.	Normal		None	7
8.	Febrile 7 days		None	12
9.	Primary healing		None	14
10.	Normal		None	9
11.	Normal		None	10

SUMMARY

Eleven cases are reported in which the patients were operated on to relieve bladder neck obstruction. Tuberculous infection was found in each of the surgical specimens.

The operative results, both immediate and late, are discussed and are shown to be comparable with results obtained in surgery of the benign prostate.

No unusual delays in healing or remarkable complications were recognized.

Three of the 4 patients who were operated on since the advent of streptomycin were given courses of the drug but no conclusions regarding its routine use are offered.

7 W. Madison St., Chicago 2, Ill.

REFERENCES

Auerbach, O.: Quart. Bull. Sea View Hosp., 7: 188, 1942.
Barney, J. D.: *J. Urol., 10: 81, 1923.*
Bothe, A. E.: J. Urol., **18**: 491, 1927.
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7 W. Madison St., Chicago 2, Ill.

REFERENCES

AUERBACH, O.: Quart. Bull. Sea View Hosp., 7: 188, 1942.
BARNEY, J. D.: J. Urol., 10: 81, 1923.
BOTHE, A. E.: J. Urol., 18: 494, 1927.
EISENDRATH, D. N. AND ROLNICK, H. C.: Urology. Philadelphia: J. B. Lippincott, 1938.

GREENBERGER, A. J.: Quart. Bull. Sea View Hosp., **7**: 123, 1942.
GREENBERGER, A. J., MONROE, E. AND WINER, JULIUS N.: Quart. Bull. Sea View Hosp., **5**: 161, 1940.
GREENBERGER, A. J., GREENBERGER, M. G. AND ALEXANDER, H.: Quart. Bull. Sea View Hosp., **1**: 425, 1936.
KOLL, I. S.: Ann. Surg., **62**: 473, 1915.
LATTIMER, J. K.: J. Urol., **59**: 326, 1948.
LITVAK, H.: Quart. Bull. Sea View Hosp., **7**: 127, 1942.
LLOYD, F., BAUMRUCKER, G. AND STONINGTON, O.: Surg. Clinics North Amer., **28**: 1639, 1948.
LOWSLEY, O. S. AND DUFF, J.: Ann. Surg., **91**: 106, 1930.
LOWSLEY, O. S. AND KIRWIN, T. J.: Clinical Urology. Baltimore: Williams and Wilkins, 1944.
McKENNA, C. H.: Tuberculosis of the urogenital tract. In: Goldberg: Clinical Tuberculosis. Philadelphia: F. A. Davis, 1947, pp. H69.
MOORE, R. A.: J. Urol., **37**: 372, 1937.
MUEHSAM, E.: Quart. Bull. Sea View Hosp., **9**: 25, 1947.
NESBIT, R. M. AND LYNN, J. M.: J. Urol., **61**: 766, 1949.
RATHBUN, N. P.: J. Urol., **57**: 285, 1947.
SCOTT, W. W.: J. Urol., **12**: 515, 1924.
SWEANEY, H. C.: J. Urol., **29**: 217, 1933.
TANNER, F. H. AND McDONALD, J. R.: Arch. Path., **36**: 358, 1943.
WALKER, G.: Johns Hopkins Hosp. Rep., **16**: 1, 1911.
WARRES, H. L.: J. Urol., **60**: 260, 1948.

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BLASTOMYCOSIS OF THE PROSTATE: CASE REPORT

R. G. BUNGE AND W. N. HARNESS

From the Department of Urology, College of Medicine, State University of of Iowa, Iowa City, Iowa

A mold-like fungus, Blastomyces dermatitidis, produces an infection called American blastomycosis. Two clinical types of infection are recognized: 1) cutaneous blastomycosis which responds to treatment, and 2) systemic blastomycosis, a highly fatal disease. The genito-urinary system is rarely involved.[1]

Our case is unusual in several respects: 1) The presenting complaint was pyuria and the fungus was first found microscopically in the wet prostatic secretion. 2) No cutaneous lesions were present although they did appear later. 3) The patient has improved on iodide therapy although, initially, pulmonary lesions were demonstrated, indicating the systemic form of the disease.

CASE REPORT

R. H., a white man aged 57, employed as a salesman, came to the urological clinic complaining of painful and frequent urinations of 4 weeks' duration. There had been no difficulty in voiding, hematuria, or upper tract symptomatology. Past history was noncontributory.

Physical examination revealed a chronically ill white man with normal skin. The head and neck were negative. The lungs contained many inspiratory wheezes. The heart was normal in size, rhythm regular and without murmurs. Blood pressure was 110/65. The abdomen and external genitalia were normal. Rectal examination indicated good sphincter tone and a moderately enlarged, firm, irregular, hot and tender prostate which, on pressure, yielded a greenish-yellow urethral discharge.

Laboratory studies: Serology was negative; blood urea nitrogen 13.0 mg. per cent; hemoglobin 11.0 gm.; red blood cells 4.1 million; white blood cells 15,600; urinalysis—pH 4.5, albumin and sugar negative; microscopic, each low power field was loaded with white blood cells and an occasional blastomycete could be found. The prostatic secretion microscopically was loaded with white blood cells and many blastomycetes were found (fig. 1). Cultures of the prostatic fluid and sputum were positive for the organism.

X-ray examinations included normal excretory urograms and a chest film which showed scattered miliary lesions interpreted as blastomycotic in type.

The patient was placed on potassium iodide and antibiotic therapy. Prostatic massage was not recommended in view of the possibility of spreading the process. His bladder irritation gradually subsided and he became more comfortable. He continued on the iodide therapy and 5 months later developed cutaneous lesions proven to be blastomycotic by biopsy. These gradually improved. Then seven months later he developed signs of chronic right epididymitis which has persisted to the present time.

Fourteen months later, he was taking 600 drops of saturated solution of

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[1] Martin, D. S. and Smith, D. T.: Am. Rev. Tuberc., 39: 275, 1939.

Greenberger, A J Quart Bull Sea View Hosp , **7:** 123, 1942

Greenberger, A J , Monroe, E and Winer, Julius N Quart Bull Sea View Hosp , **5:** 161, 1940

Greenberger, A J , Greenberger, M G and Alexander, H Quart Bull Sea View Hosp , **1:** 425, 1936

Koll, I S Ann Surg , **62:** 473, 1915

Lattimer, J K J Urol , **59:** 326, 1948

Litvak, H Quart Bull Sea View Hosp , **7:** 127, 1942

Lloyd, F , Baumrucker, G and Stonington, O Surg Clinics North Amer , **28:** 1639, 1948

Lowsley, O S and Duff, J Ann Surg , **91:** 106, 1930

Lowsley, O S and Kirwin, T J Clinical Urology Baltimore Williams and Wilkins, 1944

McKenna, C H Tuberculosis of the urogenital tract In Goldberg Clinical Tuberculosis Philadelphia F A Davis, 1947, pp H69

Moore, R A J Urol , **37:** 372, 1937

Muehsam, E Quart Bull Sea View Hosp , **9:** 25, 1947

Nesbit, R M and Lynn, J M J Urol , **61:** 766, 1949

Rathbun, N P J Urol , **57:** 285, 1947

Scott, W W J Urol , **12:** 515, 1924

Sweaney, H C J Urol , **29:** 217, 1933

Tanner, F H and McDonald, J R Arch Path , **36:** 358, 1943.

Walker, G Johns Hopkins Hosp Rep , **16:** 1, 1911

Warres, H L J Urol , **60:** 260, 1948

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Fourteen months later, he was taking 600 drops of saturated solution of potassium iodide daily without discomfort. He complained of occasional bouts of bladder irritation with pyuria, some tenderness in the right scrotal contents, but felt that his general health was better. Chest x-rays have shown slight improvement in the pulmonary lesions.

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[1] Martin, D. S. and Smith, D. T.: Am. Rev. Tuberc., 39: 275, 1939.

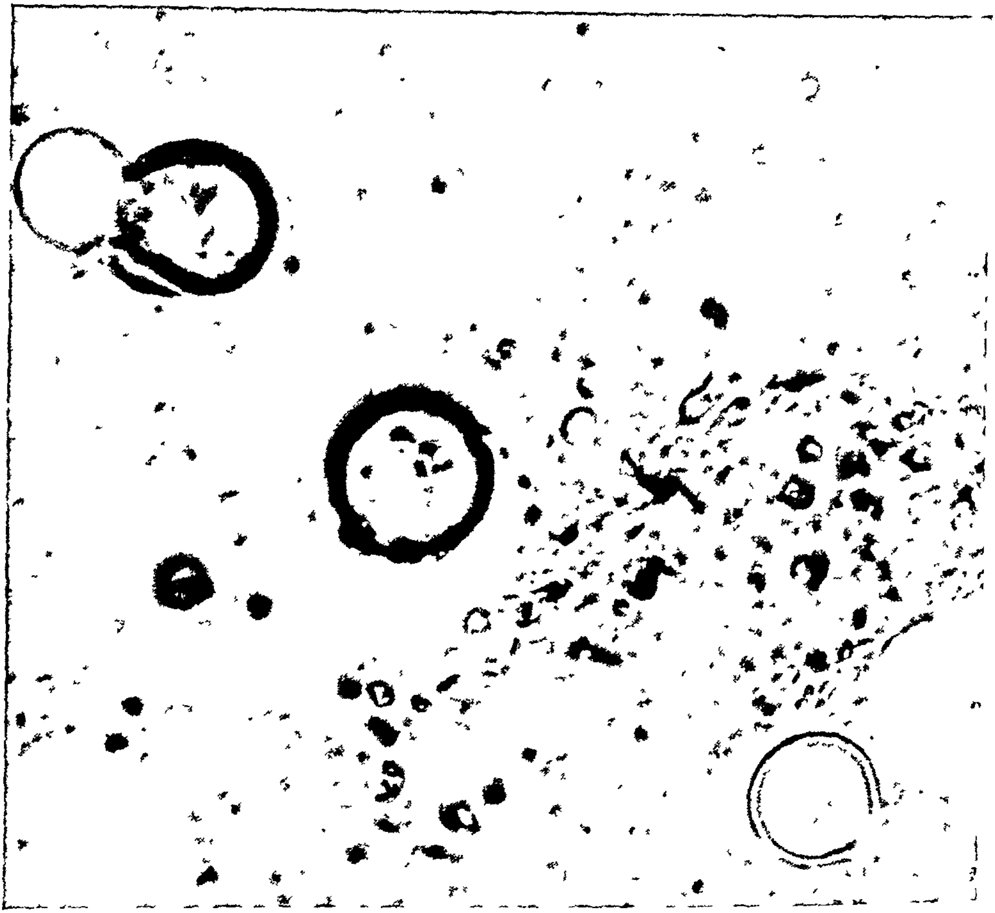

FIG 1 Photomicrograph of wet prostatic secretion showing double refractile blastomycetes

COMMENT

Moore and Halpern reported a case of prostatic blastomycosis which developed cutaneous lesions following bi-weekly prostatic massages by a physician.[2] In our case, we advisedly did not institute local massage and yet cutaneous lesions developed. However, the patient has generally improved on iodide therapy and we were reluctant to advise surgical extirpation of the epididymal focus, fearing further systemic spread.[3] Intermittent courses of various antibiotic agents have controlled the severity of the pyuria.

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[2] Moore, M and Halpern, L K J Urol , 60: 612, 1948

[3] Jacobson Jr C E. and Dockerty, M B . *J. Urol* , *50: 237, 1943*

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HEMOSTASIS IN TRANSURETHRAL RESECTIONS: THE USE OF ADRENALIN-HYALURONIDASE MIXTURE

WILLIAM BAURYS

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Intraprostatic injection of hemostatic drugs was first described by Emmett. He later discarded the procedure with the comment that it was not satisfactory for transurethral operations as practiced at The Mayo Clinic and he also stated that the method added an element of danger. Nesbit does not advocate the measure. In his opinion secondary vascular relaxation deprives it of all value.

Creevy presented his experiences in a preliminary report and enumerated its manifold advantages. Almost eight years have elapsed since Creevy's paper was published and few pertinent items have appeared in the literature since then. In spite of conspicuous numerous advantages, the procedure, in our opinion, has not been accepted with the degree of appreciation it merits. In this paper we propose to stress Dr. Creevy's observations and to present our own experience with a somewhat altered technique.

Any measure which reduces bleeding facilitates and expedites transurethral resections. The type of patient subjected to this operation requires the mildest possible postoperative reaction and a smooth convalescence, which are best achieved when bleeding is controlled. On the other hand, technical advantages to the operator are obvious.

Vasoconstricting properties of adrenalin are employed to produce hemostasis. The drug is mixed in a suitable menstruum and injected into the substance of the prostate. We have found adrenalin to be most desirable because it is least dangerous since vasoconstriction is peripheral. Coronary vessels undergo dilatation under its influence. Addition of pitressin, as recommended by Creevy, adds an element of danger since coronary vessels undergo constriction with this drug. Both Emmett and Creevy experimented with pituitrin. Because of attendant severe systemic reactions, it was classified as exceedingly hazardous. Creevy found no benefit from vitamin K, hypertonic saline, koagamin, calcium salts or fibrinogen.

The formula we have found admirably sufficient is composed of 1 cc of 1-1000 adrenalin and 100 TRU (turbidity reduction units) of hyaluronidase in 100 cc saline. These substances are compatible and dissolve readily.

In the average patient, 10 cc of this mixture is injected into each lobe of the prostate with a long needle through a Braasch cystoscope. Only one point of injection is necessary in each lobe. The total amount represents about three drops of adrenalin and thirty units of hyaluronidase.

Hyaluronidase has been added to the solution because of its "spread factor." This substance is an enzyme obtained from bovine testes and it has the property of hydrolyzing hyaluronic acid, one of the intercellular cement substances of

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Read at annual meeting, Northeastern Section, American Urological Association, Bolton Landing, N. Y., September 16, 1950.

connective tissue. This enzyme is also an important constituent of snake venom and, because of the spreading effect, the toxin acts so rapidly after a reptile bite.

Therapeutically, it is used to augment absorption of fluids given subcutaneously. We have found it useful in making urograms in infants and young children when necessary to administer the dye intramuscularly or subcutaneously. No associated systemic reaction occurs irrespective of dose.

The spreading power can be demonstrated by injecting neo-iopax into the prostate with hyaluronidase. In the first film (fig. 1, *A*), the dye without the enzyme is seen to remain in a circumscribed area, while in the second study it is spread over the entire base of the bladder (fig. 1, *B*). Both studies were made with the same amount of dye and the same interval between injection and the x-ray. The glands used for the demonstration were appraised as approximately the same in size and consistency.

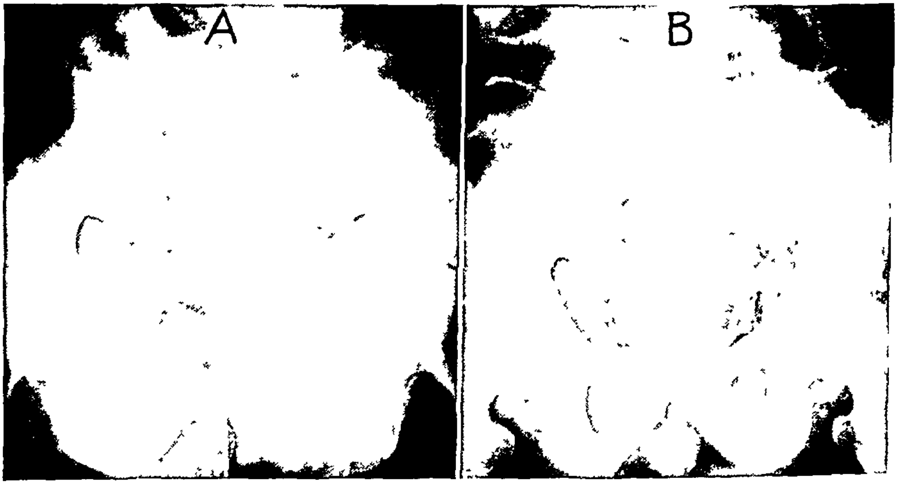

FIG. 1. *A*, injection of neo-iopax without hyaluronidase. *B*, injection after hyaluronidase.

When the vasoconstricting solution is introduced, a blanching is noted immediately. The position of the needle must be verified. If blood is aspirated, another point is selected. As the fluid is injected a certain resistance is noted and if it enters too freely, the needle has been passed through the entire substance of the gland and again the position must be altered. The bulk of the injected mixture does not distort the field.

Spreading of the active substance gives a wider and more effective distribution of the vasoconstricting ingredient. The result is much better than one produced by using multiple points of injection. We have used both Dr. Creevey's formula and our own and we find the latter is superior in the desired effect. Only two points of injection are necessary and hemostasis involves the entire gland.

After each 5 cc of injected solution, blood pressure reading is made. Any elevation occurs immediately and if a substantial rise above normal is noted, the patient is given amyl nitrite to inhale. This procedure invariably restores the normal level in a moment, and it has a tendency to remain there. Further injection of constricting solution is continued.

Following the usual drop in pressure with spinal anesthesia, the injected solution can be used to restore the difference. In an experience of over 400 such injections, we have never found any alarming reactions.

After administering the medication, the Braasch cystoscope is replaced with the resectoscope. Very little time is lost in the change-over. Although the injection can be made with the needle attachment of the McCarthy instrument, it is more difficult to manipulate. Furthermore, the needle attachment is not designed to be introduced into the Nesbit resectoscope, which we prefer to use.

Another maneuver is to introduce a ureteral catheter through a biopsy needle by way of the perineum. In this manner, fractional doses are added as necessary. Recently, we have chosen to remove the larger hypertrophies by the retropubic method. Prostates appraised as over 70 grams are approached by the open method.

The length of time hemostasis remains, varies with different patients. Although the field is absolutely bloodless for only 12 to 15 minutes, hemostasis remains to a satisfactory degree for as long as 40 minutes. In a small number of instances, the result is almost negligible. Just why, I don't know. A few patients are sensitive to adrenalin and this is observed after the first 5 cc of the mixture is administered. These individuals begin to breath rapidly and complain of a consciousness of a severe heart pounding. Such a reaction precludes further injection. We have observed no other contraindications. If the gland is of modest size or if the pressure has a tendency to rise abruptly, only 5 cc are injected into each lobe.

In spite of the amount of tissue resected, hemorrhage is comparatively small compared to resections which are done without intraprostatic injections. A 300 cc blood loss is quite high and unusual. Occasionally, in larger glands, a loss of 5 cc per gram is noted; loss in larger glands is 3 to 4 cc per gram. In observations on bleeding during resections in 92 cases of prostatic obstruction, Nesbit found 4 to 1254 cc for an average of 8.4 cc per gram. Pilcher in a similar study noted an average loss of 29 cc per gram. In our own experience, with 132 cases before the use of hemostatic substances, the loss measured 11 cc per gram. In larger glands, of course, per-gram-loss is always higher. In the more numerous small glands, hemostasis is particularly effective. In the hands of the less dextrous operator, even small resections are attended with considerable blood loss.

About one third of all resections weigh a maximum of 15 gm. About 90 per cent weigh 70 gm. or less. Over one half weigh a maximum of 30 gm. and about 80 per cent weigh up to 50 gm. These figures are adduced from our own experience and from reports in the literature.

In reviewing the size of obstruction encountered, in our opinion hemostatic solution is applicable in at least 80 per cent of all prostatic transurethral operations. Small glands weighing a maximum of 15 gm. may be removed with a blood loss of less than 30 cc. This, of course, means one third of resections can be done with almost a negligible loss of blood. Furthermore, a substantial number of prostates weigh up to 30 gm. and these too may be resected with a small amount of hemorrhage. It is unusual to lose more than 2 cc per gram in grade 1 resections. Any loss up to 30 cc is negligible, consequently resections in which the connective tissue. This enzyme is also an important constituent of snake venom and, because of the spreading effect, the toxin acts so rapidly after a reptile bite.

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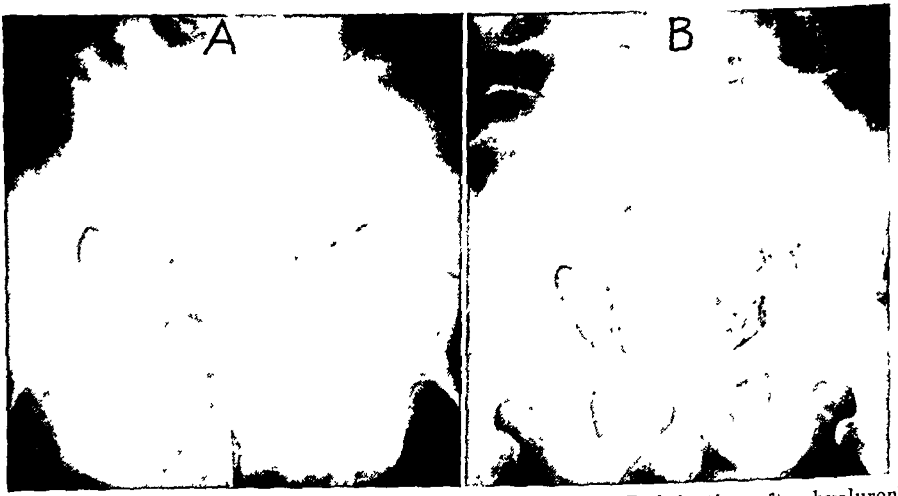

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The following charts show blood loss recorded with and without intraprostatic injection in glands of various sizes:

With Hemostatic Injection

No. of resections	*Amount of tissue*	*Blood loss*
28	Up to 15 gm.	All less than 30 cc
36	16 to 30 gm.	Only 5 above 30 cc
36	31 to 75 gm.	4.5 cc per gram
100 Total		

Without Hemostatic Solution

36	Up to 15 gm.	5.2 cc per gram
24	16 to 30 gm.	9 cc per gram
40	31 to 100 gm.	12.4 cc per gram
100 Total		

In the hands of the more skillful operator, blood loss in resections weighing up to 30 gm. represents only a small one even without hemostatic agents, but this is not universally so. Observation in glands weighing 30 gm. without intraprostatic injection revealed 9.4 cc per gram blood loss among 44 such prostates. With the use of hemostatic solution, under similar conditions, average loss was approximately 1.2 cc per gram.

Use of hemostasis will depend on individual experience and proficiency. The expert transurethral resectionist spurns the idea because he is able to work rapidly and to efficiently control bleeding while operating on modest sized resections. We take no issue with the premise that the best way to control bleeding is by coagulation. Since a substantial number of transurethral resectionists do not fall into the expert class, use of hemostasis will expedite the operation even in smaller prostates.

Advantages of this method are obvious. These older men undoubtedly are much more sensitive to attendant reactions following loss of large amounts of blood. Morbidity is definitely reduced.

To the operator, advantages of an almost bloodless field are numerous. Frequent and prolonged interruption of the operation to coagulate bleeders is not required. The operative field may be viewed through a relatively clear medium and tissues more easily identified. It is unnecessary to appraise the prostatic area through a heavy red fog.

The height of the percolator can be held at a minimum level above the patient and a smaller amount of irrigating fluid is required. Such conditions reduce tendency toward excessive intravascular hemolysis. Determinations of hemoglobinemia by the Evelyn electronic colorometer show only a small degree of intravascular hemolysis when the hemostatic agent is used. This fact is not so important now that glycine and 4 per cent glucose have almost entirely replaced distilled water as irrigating agents. Necessity for postoperative transfusions is notably reduced.

The question naturally arises about secondary relaxation. We have observed neither more nor less postoperative bleeding than without use of hemostasis. Secondary vascular relaxation has not been a deterring factor in our hands. Bleeders are treated in the usual manner as hemostasis relents.

An issue may also arise about the use of the "spread factor" substance in carcinomatous glands. Although we have nothing of a definitive nature to offer along this line, so far we have observed nothing in the way of a discouraging effect. Theoretically, the transurethral procedure itself might be condemned because of such potential tendencies; however, empirically, results do not substantiate the contention.

SUMMARY

The advantages of hemostasis during transurethral resections are discussed.

Experiences with a new hemostatic solution containing hyaluronidase is described.

The resulting blood loss in resections of various sizes with and without hemostatic solution are tabulated.

REFERENCES

Creevy, C. D.: J. Urol., 50: 593–597, 1943.
Emmett, J. L.: Proc. Staff Meet. Mayo Clinic, 11: 619–622, 1936.
Nesbit, R. M. and Conger, K. B.: J. Urol., 46: 713–717, 1941.
Nesbit, R. M.: New Eng. J. Med., 207: 214, 1947.
Pilcher, J. F. and Sheard, C.: Proc. Staff Meet. Mayo Clinic, 12: 207–213, 1937.

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RUPTURE OF THE TESTICLE

LOWRAIN E. McCREA

Traumatic rupture of the testicle without laceration of the scrotal skin is a rare condition.

A review of the literature has revealed a total of 12 previously reported cases. The first case was presented by Cotton in 1906. Since that time the reports of the remaining 11 cases have sporadically appeared in the literature. A thirteenth case is herein reported. Little mention is made of the condition in our texts. No reference could be found as to what procedure was considered to be the proper method of surgical management. An analysis of the presented cases show that 8 were treated by orchiectomy and 4 were treated by closure of the tunica albuginea. Rupture of the testicle when mentioned in our texts is discussed under the subject of contusions. Terrillon and Suchard, in discussing the subject, divide testicular injury into three types: those in which there are disseminated capillary hemorrhages between the seminiferous tubules; those in which the hemorrhages are the size of a pea to that of a cherry, and lastly those in which the tunica albuginea itself is ruptured with bleeding into the tunica vaginalis. It is the last type that is to be considered. It is believed that the condition is of sufficient importance to be considered as an individual clinical entity. An analysis of the previously reported cases shows the defect in the tunica albuginea to be quite extensive. The testicular tubules are herniated within the tunica vaginalis. In some instances the testicular substance was completely shattered. In others the testicular substance was intact but protruded through a tear or rent in the tunica albuginea.

The testicles, suspended and protected as they are, are seldom traumatized but occasionally are subject to direct force or sudden pressure. An analysis of the 13 cases to be found in the literature disclosed that all cases of trauma were caused by impacks of a direct nature. Further analyzing the nature of the accident of the reported cases, it would appear that in all the cases the blow was directed upward or obliquely upward. A blow directed in this manner would cause the testicle to be impinged between the symphysis pubis or the thigh and the striking object, regardless of its nature. This may be clearly seen in an analysis of table 1. In not a single instance in which rupture was reported was the scrotum or testicle struck by a soft object. In every instance pain was an immediate symptom. It is interesting to note that the age at which the accident occurred was during the span of life of greatest physical activity, the youngest being 8 years and the oldest 49 years of age. The average age was 23 years. It is recognized that the testes are remarkably sensitive to slight trauma. Trivial injuries to the testes (without rupture) are frequently associated with nausea, vomiting or even shock. It was surprising in an analysis of the cases presented to find only 3 instances of shock. It is interesting to note that shock when present in instances of rupture of the testicle was evident to a minor degree. The

TABLE 1

NAME	AGE	ACCIDENT	PAIN	SHOCK	SWELLING	VOMITING	OPERATION
Cotton, 1906	47	Struck with baseball	Immediate then subsided	Immediate Slight	Increasing	Yes	Orchiectomy
Malapert, 1916	17	Kicked by horse	Immediate Severe	No	Hydrocele, 1 month	No	Bottle operation
Campbell, 1937	8	Fell astride foot board of bed	Marked	No	Yes	Not mentioned	Suture of tunica albuginea
Navarrette 1937	30	Fell astride metal hand rail	Slight	No	Increasing	Not mentioned	Orchiectomy
Navarrette 1937	27	Struck by belt buckle	Intense	No	Increasing	Not mentioned	Orchiectomy
Castro, 1940	16	Struck by knee playing football	Severe radiating pain	No	Yes	No	Orchiectomy
Castro, 1940	27	Blow to scrotum while playing football	Severe pain	No	No	No	Orchiectomy
Sejournet, 1944	21	Kicked in scrotum	Immediate but subsided	Yes	Gradual	No	Orchiectomy
Counseller and Pratt, 1944	17	Struck during basketball game	Slight	No	Gradual swelling	No	Closure tunica albuginea
Wesson, 1946	49	Struck by handle of sledge hammer	Immediate	Slight	Gradual	No	Closure tunica albuginea

TABLE 1—*Continued*

NAME	AGE	ACCIDENT	PAIN	SHOCK	SWELLING	VOMITING	OPERATION
Senger, 1947	28	Kicked in scrotum	Tenderness	No	Increasing	No	Orchiectomy
Senger, 1947	16	Kicked by horse	Severe	No	Gradual increase	No	Orchiectomy
McCrea, 1950	16	Struck by baseball	Pain immediately—lasted 1 hour	No	Gradual	No	Modified bottle operation

shock was immediate, slight, temporary. The case presented by Cotton is the only one which developed immediate shock and vomiting following trauma.

The symptoms universally portrayed by patients having traumatic rupture of the testicles were immediate pain, which usually subsided, followed by gradual increasing swelling of the scrotum. The usual preoperative diagnosis made was that of an hematocele. Such a diagnosis was made due to continuous bleeding with increasing size of the scrotum. The diagnosis of hematocele has been made frequently by surgeons and urologists for many years. Any number of these cases could well have been rupture of the testicle but apparently stopped bleeding and were followed by gradual resolution. These cases were lost and the end results will never be known. Whether atrophy of the testicle ultimately occurred or glandular acitivity normally continued cannot be ascertained. It is the writer's conviction, since observing the case to be presented and after having analyzed the previously reported cases, that the scrotum should be surgically opened and the testicle should be examined in every instance in which there is a history of trauma and in which a diagnosis of a hematocele is made.

It is further interesting to note that in 4 instances the tunica albuginea was closed by suture and the testicle permitted to remain. Campbell stated that atrophy of the testicle was not apparent in his case 7 years following surgery. This is in direct contrast to the statement of Reclus who dogmatically stated that when the torn tunica albuginea was sutured and not removed, atrophy of the testicle occurred within 6 weeks. It is regrettable that the end results of the other 3 cases in the literature were not mentioned.

CASE REPORT

T. R., a 16 year old white boy was struck by a thrown baseball on June 11, 1950. The ball struck the ground, bounced and struck the scrotum. The accident happened about 3 o'clock in the afternoon. He immediately became nauseated but did not vomit. There was no evidence of shock. He experienced slight pain in the right testicle, which pain continued for about 1 hour. He walked home without discomfort and ate a normal evening meal. He noticed that upon removal of his jockey shorts the pain recurred. He retired about 9:30 p.m., but was unable to sleep because of constant pain in the testicle. There was a slight swelling of the scrotum. He went to school as usual the next day. He stated he was comfortable as long as the testicles were supported or not compressed by his clothing in any way. He was unable to sleep that night because of dull, constant pain in the testicle. The swelling was relatively the same as 24 hours previously.

He was seen 48 hours after the accident by his family physician. At that time there was a globular mass about the size of a small orange in the scrotum. The testicle was palpable above the mass and was somewhat tender to palpation. He was treated by hot sitz baths and the use of a scrotal suspensory. He did not complain of any further pains. He played baseball on several occasions, was swimming and diving on 2 occasions and worked as a janitor's assistant for several days. The swelling within the scrotum gradually increased.

When first seen on June 27, 1950, there was a mass in the scrotum about the size of a large orange. The mass was not translucent. The testicle was palpable above the mass and tender to palpation.

On July 10, 1950, one month following the accident, the scrotum was opened and a large quantity of blood was evacuated from the tunica vaginalis. An area of capillary bleeding on the wall of the tunica vaginalis was observed and ligated. The tunica albuginea presented a transverse rupture about 4 cm. in length. There was no evidence of bleeding from the testicle. It was impossible to satisfactorily close the rent in the tunica albuginea without making excessive pressure on the testicular substance. The tunica vaginalis was partially resected and a modified "bottle operation" done. Recovery was uneventful.

CONCLUSIONS

A case of traumatic rupture of the testicle is presented making the thirteenth case reported in the literature.

Review and analysis of the 13 cases reflect the typical symptomatology of pain of varying degrees and swelling of the scrotum due to a hematocele. Severe shock is not a usual symptom of rupture of the testicle. Mild shock was noted in but 3 instances of the 13 cases reported in the literature.

Atrophy of the testicle does not always follow conservative surgical measures in the treatment of rupture of the tunica albuginea.

Exposure and examination of the testicle are advised in every instance of trauma to the scrotum or its contents in which a hematocele immediately or gradually occurs.

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REFERENCES

Campbell, M. F.: Pediatric Urology. New York: Macmillan Co., 1937, vol. 2, p. 188.
Castro, H. D.: Rev. argent. de urol., 9: 32, 1940.
Cotton, F. J.: Am. J. Urol., 2: 587, 1905-06.
Counseller, V. S. and Pratt, J. H. Jr.: J. Urol., 52: 334, 1944.
Malapert: Gaz. Med. de Par., 87: 15, 1916.
Navarrette, E.: Rev. mid. Peruana, 9: 271, 1937.
Sejournet, M. P.: Bull. et mem. Soc. d.chirurgens de Paris, 35: 101, 1944.
Senger, F. L., Bottone, J. J. and Ittner, W. F.: J. Urol., 58: 453, 1947.
Wesson, M. B.: Urol. & Cutan. Rev., 50: 16, 1946.

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TORSION AND RUPTURE OF AN INTRA-ABDOMINAL SEMINOMA

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It has been estimated by Campbell that in 20 per cent of all cases of cryptorchidism the testis does not leave the abdomen. A testis so situated may be occupied by a new growth. It may be recognized clinically on occasions particularly when torsion occurs. We wish to report such a case and to review the literature on the subject.

CASE REPORT

M. G., a man aged 38, was admitted to The Jewish General Hospital on February 17, 1949, complaining of cramp-like peri-umbilical pain of 3 days' duration. His temperature was 101F, the pulse rate 112 per minute. His abdomen was everywhere moderately sensitive. Tenderness was most marked in the right lower quadrant, which was occupied by a mass. Here there was defense musculaire. The left scrotum was empty. The leukocytes numbered 13,000 per cubic millimeter, the hemoglobin was 61 per cent. The preoperative diagnosis was acute suppurative appendicitis with perforation and localized abscess formation.

Under spinal anesthesia, the mass already referred to was again palpated. It was found to be smooth, regular and movable. Signs of free fluid were present. A right transverse incision was made at the level of the anterior superior spine. When the distended peritoneum came into view, blood could be seen shining through it. When the peritoneal cavity was entered a quart of dark blood escaped. The mass was palpated. It was demonstrated to have its origin on the left side of the abdomen. The transverse incision was extended, for the possibility that one was dealing with torsion and rupture of an intra-abdominal testis suggested itself. The left inguinal canal was free of contents.

A large placenta-like mass, the seat of a tear, was delivered. The long, 2 inch wide pedicle which arose from retroperitoneal tissue exhibited three clockwise twists. These were undone and the pedicle ligated. The remainder of the abdomen appeared normal. A subsequent Friedman test was negative. The postoperative course was complicated by bilateral saphenous phlebitis.

Pathologic report: The specimen (fig. 1) consisted of a large, ovoid, encapsulated structure which measured 16 by 15 by 9 cm. On one of its aspects there was a ragged tear 3 cm. long. The outer surface of the mass was relatively smooth, glistening and bluish-grey in color. The underlying vessels were numerous, branched, prominent and engorged. Several firm, raised, rounded nodules, the largest of which measured 1.5 cm. in diameter, were noted on the mass.

At one pole there was a smooth, elongated rounded ridge measuring 15 cm. in length. It had a diameter of 3.5 cm. and projected 1.5 cm. above the surface.

Between the outer aspect of the mass and the ridge there was a sulcus reminiscent of that found between a testis and the body of the epididymis.

Upon section the firm wall of the mass appeared greyish-black in color. It varied in thickness from 1 mm. to 1 cm., and was the seat of extensive hemorrhage. The interior of the mass was filled with fragmented friable reddish-brown and purple spongy material. Firmly attached to the inner wall were elevated brownish masses which projected in a papillary fashion.

Sections taken from various situations show in all extensive interstitial hemorrhage and necrosis of both the wall and contents of the cystic mass. Where the section includes portions of the friable necrotic tissue from within the cyst, the "ghost-like" outlines of a richly cellular tissue can be identified. No tubular structures are noted. In one such area (fig. 2) a few cells are moderately well preserved. They contain round, slightly vesicular nuclei which vary in size and shape and give the general impression of a tumor of the seminoma type. Sections taken through the elevated ridge-like structure described in the gross, shows in one situation poorly preserved tubular structures lined by necrotic and partially autolysed cells which in general appearance suggest epididymis. Careful search throughout all sections fails to reveal any recognizable seminiferous tubules.

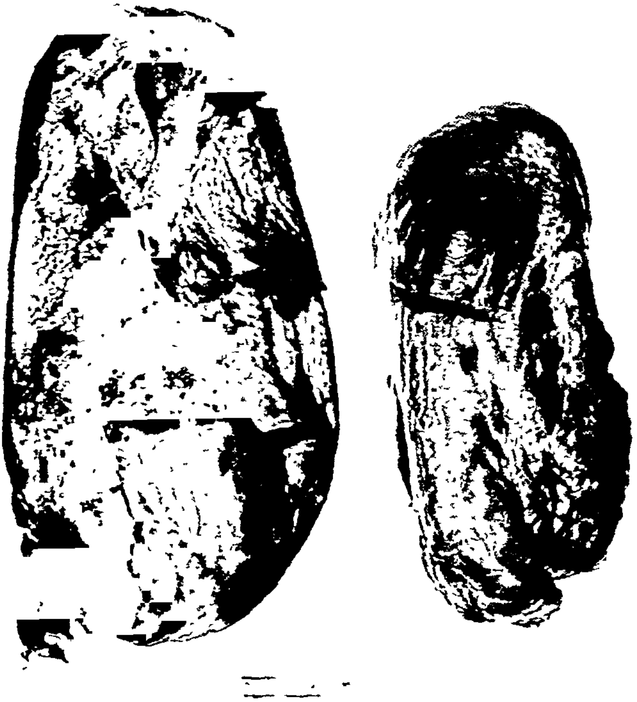

FIG. 1. Portion of specimen on left shows extensive hemorrhage and necrosis which had occurred in tumor. On right, elevated ridge is epididymis.

Diagnosis: Strangulated, necrotic, intra-abdominal testicular tumor, probably seminoma.

Comment: In only the ridge-like structure noted, is a tubular apparatus identifiable. It may represent the epididymis. The necrotic, though richly cellular tissue making up the bulk of the intracystic mass in most situations, is unsuitable for histologic interpretation. But the uniformity of the cells together with a few viable cells strongly suggest that this lesion is a seminoma.

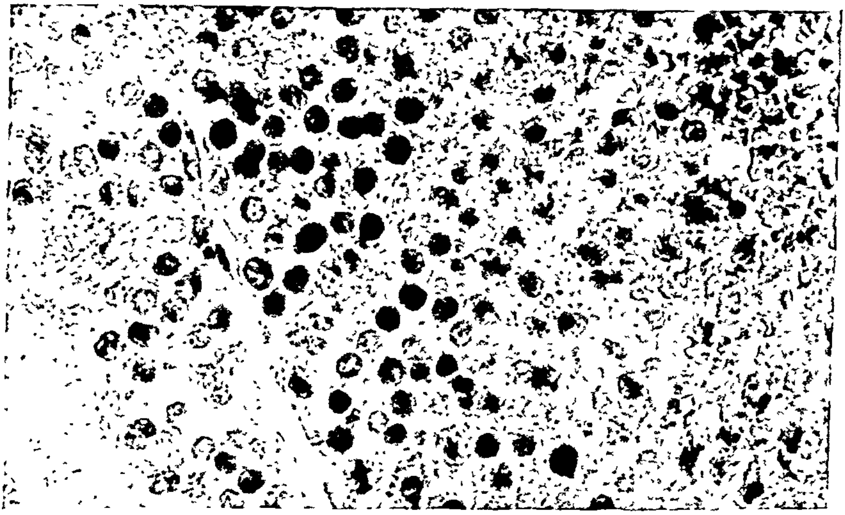

FIG. 2. Showing only portion of viable cells. Unicellular type strongly suggests seminoma. High power view, × 500.

TABLE 1

Dean	1935	13.5%
Mujagi	1938	12.4%
Hinman	1933	12.2%
Rubaschow	1926	11.0%
Rea	1931	10.0%
Gordon-Taylor	1938	13.1%

Taken from Campbell.

These sections were submitted to Dr. Charles Huggins of the University of Chicago. He and his associates were of the opinion that the histologic findings were compatible with a diagnosis of a seminoma.

DISCUSSION

Maldescent of the testis and its relationship to primary testicular tumors has been the subject of statistical surveys. The incidence of testicular neoplasms in all cases of cryptorchidism has been noted by Campbell (table 1).

Campbell also points out that the proportion of abdominal to inguinal testes is *approximately* 1:4. The incidence of abdominal and inguinal malignant growths is equal. The chances, therefore, of an abdominal testis undergoing malignant transformation are four times greater.

The occurrence of malignant disease in the intra-abdominal testis is of interest because of the rarity and the difficulty of early establishing the correct diagnosis. The development of a tumor in an intra-abdominal testis is infrequent. Torsion of such a testis is even less frequent. Beller was able to find reports of 10 cases of torsion of an intra-abdominal testis. He added another. Five revealed associated malignancy. Whittington in 1943 reported another case associated with transposition of the viscera.

We have been able to collect 7 additional reports and have added a case (table 2). In 13 or 65 per cent of the 20 cases of torsion of an intra-abdominal testis there was evidence of malignancy; in one instance (Key), bilateral.

TABLE 2 *Recorded instances of torsion of intra-abdominal testes*

NO	AUTHOR	YEAR	AGE	SIDE	DURATION OF SYMPTOMS	ECTOPIA TESTIS	ASSOC MALIGNANCY	PATH. DIAG
1	*Gerster	1897	21	R	3 days	Bilat.	Yes	Not given
2	*Stiles	1905	39	R	3 days	Unilat.	Yes	Sarcoma
3	*Leconte	1907	28	R	10 days	Unilat.	Yes	Sarcoma
4	*Howard	1907	15	R	2 days	Bilat.	No	
5	†Key	1914	25	Bil.	2 days	Bilat.	Yes	Sarcoma
6	*Cupler	1915		R		Unilat.	No	
7	*Ormond	1927	42	R	2 days	Unilat	No	
8	*Pearlman	1927	18	L	10 days	Unilat	Yes	Not given
9	*Wallenstein	1927	33	L	1 day	Bilat.	No	
10	†Birukov	1928	14	L	"weeks"	Unilat.	No	
11	†Jonnson	1933	27	R	2 days	Unilat	Yes	Carcinoma
12	*Power	1933		L		Unilat.	No	
13	*Chitty	1933				Unilat.	Yes	Not given
14	Vastola	1933				Bilat.	Yes	Embyonal
15	*Beller	1934		L		Unilat	No	
16	†Jossa	1935	23	L	3 weeks	Unilat	Yes	Sarcoma
17	Burke	1938				Unilat.	Yes	Not given
18	Whittington	1943				Unilat.	Yes	Not given
19	Bennett & Shaw	1947	38	R	2 days	Unilat	Yes	Not given
20	Authors' case	1949	38	L	3 days	Unilat	Yes	Seminoma

* Cited by Beller.
† Cited by Jossa

Bulkley found that in general hospital male admissions, malignant disease of an abdominal testis is seen once in 60,000 admissions.

Whether all undescended testes are potentially malignant remains a debatable point. Gilbert and Hamilton noted that in 11 per cent of recorded cases of testicular carcinoma there is a concomitant ectopy; a correlation approximately 50 times higher than could be expected by chance association. Patients with carcinoma of the testis commonly reveal congenital defects such as hernia and pseudohermaphroditism. Bennett-Jones and Harrison record a case of seminoma of an abdominal testis with glioma of the brain.

In patients with carcinoma of one testis and unilateral cryptorchidism, the neoplasm occurred in the undescended testis in 97.5 per cent of the cases. In patients with bilateral cryptorchidism and unilateral testicular malignancy, 24.6 per cent subsequently developed carcinoma in the second undescended testis, whereas in patients whose testes were both in the scrotum, malignancy in one testis was followed by the development of carcinoma in the other testis in 0.76 per cent of cases. Thus the frequency of bilateral malignant involvement of ectopic testes is 32 times that of the scrotal testis. Even in men who are not cryptorchids the possibility of involvment of the second testis after the occurrence of carcinoma in one testis is 770 times the incidence of carcinoma in either testis of the general male population.

In view of the frequency of malignant disease in the undescended testis Gordon-Taylor and Till sought to ascertain whether or not orchidopexy tends to prevent such susceptibility. They reported two instances in which malignancy occurred in the testis following orchidopexy and one after the testis had been replaced in the abdomen. It is the opinion of Cabot that successful orchidopexy minimizes this danger.

Gilbert and Hamilton do not believe that ectopy hastens the development of carcinoma. Malignancy appears at an earlier average age in patients with scrotal than with ectopic testes; 31 as compared with 34 years of age. It is doubtful if this age variation is statistically significant. Cognizance must also be taken of late diagnosis. No particular tumor type is favored by the ectopic site.

In the relatively few cases reported, the right testis appears to be involved more often than the left. The torsion is responsible for the objective manifestations of an "acute abdomen," erroneously attributed to acute appendicitis.

SUMMARY

A case of torsion of an intra-abdominal testis, the seat of a seminoma, is reported. Thirteen or 65 per cent of all cases of torsion of an intra-abdominal testis reported to date were associated with malignancy, in one instance bilateral.

REFERENCES

Beller, A. J.: Torsion of an intra-abdominal testicle. Ann. Surg., **102:** 41–48, 1935.

Bennet-Jones, M. J. and Harrison, C. V.: Seminoma of abdominal testis with glioma of brain. Brit. J. Surg., **28:** 357–61, 1940–41.

Bennett, A. H. and Shaw, W. G.: Case of undescended testis with seminomatous change and torsion. Brit. Med. J., **1:** 256, 1947.

Bulkley, K.: Malignant disease of testicle retained within abdominal cavity. Surg., Gynec. & Obst., **17:** 703-719, 1913.

Burke, J.: Torsion of pedicle of intra-abdominal seminoma. Zentralbl. f. Chir., **65:** 2821-2822, 1938.

Cabot, H. and Berkson, J.: Neoplasms of testis. Study of results of orchidectomy with and without irradiation. New England J. Med., **220:** 192–195, 1939.

Campbell, H. E.: Incidence of malignant growths in undescended testis. A critical and statistical study. Arch. Surg., **44:** 353–369, 1942.

Gilbert, J. B. and Hamilton, J. B.: Studies in malignant testis tumors. Incidence and nature of tumors in ectopic testes. Surg., Gynec. & Obst., **71:** 731–743, 1940.

Gordon-Taylor, G. and Till, A. S.: Neoplasms of undescended organ. Brit. J. Urol., **10:** 33–45, 1938.

Gordon-Taylor, G. and Wyndham, N. R.: On malignant tumors of testicle. Brit. J. Surg., **35:** 6–17, 1947.

Josa, L.: Torsion of pedicle of an abdominal testis. Beit. z. klin. Chir., **163:** 45–50, 1936.

Murray, O. B. and Ewert, E. E.: Malignant disease in undescended testes: S. Clin. North Amer., **27:** 709–713, 1947.

Nesbit, R. M. and Lynn, J. M.: Malignant testicular neoplasms. Analysis of 80 cases. Surg., **20:** 273–279, 1946.

Vastola, A. P.: Embryonal carcinoma of an abdominal testis in a pseudohermaphrodite. J. A. M. A., **101:** 111–114, 1933.

Whittington, C. T.: Case of undescended intra-abdominal testicle with torsion of the cord and embryonal cell carcinoma. Am. J. Surg., **60:** 304–305, 1943.

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RESULTS OF SURGERY IN TUMOR OF TESTIS, ESPECIALLY RADICAL REMOVAL

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Since the introduction of more modern methods of anesthesia, supportive intravenous fluids and with newer chemical agents, especially antibiotics, there has been an increase in the removal of widespread fascia and lymph areas with carcinomas of the various organs of the body. Among these, tumors of the testis offer an opportunity for removal of the tumor and its fascial and lymph planes likely to be involved. For that purpose a review has been made of the testis tumors treated at the Squier Clinic since 1928 with special reference to the results obtained by radical removal of the tumor.

The earliest proponents of radical surgery for the testis were Chevassu in France, and Young and Hinman in the United States. Hinman reviewed the subject in 1933 and showed that few surgeons had performed the operation a sufficient number of times to be able to judge its feasibility and the results. He also showed that most surgeons attempted removal when metastases were already so extensive that no reasonable operative procedure was possible to remove all the metastases. To a reader of his report several questions would seem pertinent. First, why were metastases not discovered before the operative procedure was attempted? Also, if metastases could not be shown, was that the criterion for proceeding with the radical operation? The logic would be that if no metastases were demonstrated, removal of the lymph and fascial planes may have only microscopic metastases and offer the best chance for complete removal. If metastases were demonstrated grossly, then even if removed the prognosis would be poor because then there might be microscopic metastases beyond that area.

Before the Hinman report, we had performed a number of radical removals but in several found metastases impossible to remove. After this experience, a study then was made of all cases in which the patients were or were not subjected to radical removal to ascertain, if possible, whether metastases were demonstrable. From reported cases it is apparent that the common tumors of the testicle more often form metastases by way of the lymphatics. Teratogenous tumors are thought to metastasize earlier than seminomas. Metastases of both at times may be early but more often the tumor may be present for a considerable period without spread. Metastases do occur by way of the blood stream but less frequently and may give rise at times to generalized metastases without involving the primary lymphatics. The primary lymphatics of the testicles drain along the spermatic vessels, cross the ureter and empty into the lateral lumbar nodes. These lie lateral to, around, and in front of the large vessels below the renals. The chain of nodes into which they empty extends from the common iliac to the renal vessels. The secondary lymphatics drain into 1) the

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primary nodes on the opposite side, 2) nodes behind and between the great vessels above and below the renals. Extension from these nodes may be to and through the mediastinal and to the supraclavical group. Involvement of the lungs may occur by lymphatics or by the blood stream appearing as spheroid masses, denser than normal lung tissue. General metastases may occur in the liver, facial bones, intracranially and in various places. Testicular tumors rarely break through their scrotal fascial coverings and invade locally. Extension to the scrotum has been seen with exploratory puncture or ill advised incision into the tumor. Only when these unusual fascial invasions occur, does one see involvement of the inguinal nodes, or rarely these nodes are involved late by retrograde flow after the retroperitoneal nodes are blocked with tumor infiltration. The work of Lewis and his co-workers in the Army has added greatly to the knowledge of the timing and rate and place of metastases of these tumors.

Stereographic thoracic x-rays have long been the means of determining metastatic involvement of the lungs and mediastinum. Abdominal x-rays are also the best means of determining whether involvement of the fascial planes and the lumbar nodes is present. Unexplained shadows, alteration of, or changes in the outlines have been shown to be due to metastatic involvement. Excretory urograms have shown effects upon the pelvis, distortion or displacement and at times obstruction of the ureter by metastases. The deductions drawn from our studies in these cases are that abnormal shadows or changes from the normal when associated with testicular tumor were most often due to metastases.

A study was made also to determine whether hormone tests were helpful in establishing the presence of metastases. The finding of hormone excretion in the urine of a patient with a testicular tumor shows 1) the presence of hormonal secreting cells and 2) may show the amount of secretory activity of cells in tumors such as choriocarcinoma or the cellular bulk present in the less actively secreting teratoma. Thus the presence of a large amount of hormonal excretion with a small testicular tumor would imply an actively secreting tumor or many secreting cells elsewhere than the primary tumor. If no metastases are demonstrable it would be more probably from the primary tumor, probably a choriocarcinoma. By itself the presence of the hormone is no criterion for determining whether metastases are present. After the primary tumor is removed an abnormal high hormonal excretion is evidence that secreting metastatic cells are present somewhere else.

We have selected from testicular tumor cases available since 1928, ninety-three cases for study. Other cases have been hospitalized during that time, but some with demonstrated metastases were treated only by the radiotherapy department and were not included. In others, sufficient follow-up data were not available. The 93 cases studied passed through the department of urology for surgical consideration. The follow-up data were those that were available at the time of study. The treatments fell into the following catagories: 1) x-ray therapy only; 2) removal of the testis with a scrotal incision first and then inguinal, and followed by x-ray therapy; 3) removal of the testis through an inguinal incision; 4) removal of the testis through an inguinal incision followed by x-ray therapy;

5) radical removal of the testis; 6) radical removal of the testis followed by x-ray therapy.

X-RAY THERAPY ONLY

Five cases were treated by x-ray only, all presenting a tumor in the scrotum and demonstrable masses in the abdomen or shadows in the chest interpreted as metastases. Of these 5 cases, 2 patients died in 1 year and 1 died in 2 years. One patient with tumor of an undescended testis saw recession of his tumor under x-ray, but 5 years later developed malignant hypertension which was associated with an x-ray fibrosed kidney on the involved side. Removal of the kidney relieved the hypertension and the patient is now well and free from recurrence for 10 years. One case with a testicular mass and supposed metastases and a strongly positive Wassermann was treated by x-ray and antiluetic treatment and is alive for 13 years. These 2 patients alive never had had carcinoma proved by pathological specimen.

REMOVAL OF THE TESTIS WITH A SCROTAL INCISION FIRST, THEN AN INGUINAL INCISION FOLLOWED BY X-RAY THERAPY

Four patients were operated on through the scrotum, and then the diagnosis discovered. These cases had transilluminating hydroceles and on exposure of the testis, the tumor was found. All then had inguinal removal of the cord and the scrotal contents. Immediately subsequent to the operation the patients were subjected to x-ray therapy. Two patients died a year after the operation. One was followed for a year without demonstrable metastases, and then lost to follow-up. One was followed for 2 years without change.

INGUINAL INCISION BUT NO X-RAY THERAPY

Nine patients were so treated. X-ray therapy was either refused by the patient or considered unnecessary by the surgeon in the adult teratomas and the interstitial cell tumor. One patient who had a malignant tumor died in 1 year. One patient was followed for 3 years, one for 5, one for 6, and one for 16 years. Among these 5 cases of malignant tumor, there was 1 death and 4 survived over 3 years. One of these patients was a severe tabetic in whom the tumor was discovered in correcting a large hydrocele that extended into the inguinal canal. Of the 4 "benign" tumors, one, an interstitial tumor, is alive and well 4 years later and the 3 adult teratomas have been followed for 4, 7 and 20 years.

INGUINAL INCISION FOLLOWED BY X-RAY THERAPY

Forty-three patients were treated. Of these, 23 are known to be dead. Eighteen died in 1 year, 4 in 2 years and 1 in 4 years. These patients often had some metastases shown at the time of orchiectomy, and the poorest prognosis. The remaining twenty may or may not have had metastases demonstrated or suspected at the time of operation. One has been followed for 18 years, one for 17, two for 15, one for 12, one for 9, one for 8, one for 7, one for 6, one for 5, three for 4, one for 3, and 3 for 2 years. In this group we had the largest number of cases that were lost to follow-up during the war years

RADICAL REMOVAL BUT NO X-RAY THERAPY

Three patients refused x-ray therapy following radical removal. One has been followed 20 years, one for 8 and one for 7 years, all free from apparent metastases or recurrence.

RADICAL REMOVAL FOLLOWED BY X-RAY THERAPY

Twenty-six patients were treated in this manner. Of these, 6 are dead. Four of these done in the early part of the study had metastases present in the secondary areas at the time of the operation. All four died in 1 year from metastases. One patient done later with no evident metastases in the secondary lymphatics died in 2 years with diffuse metastases through the secondary lymphatics. One patient died in 14 years with metastases in the secondary lymphatics. The remaining 20 patients have been followed practically to date and the data are most accurate. Two are alive 20 years; one, 19; two, 18; one, 17; two, 13; three, 12; one, 11, one, 10; one, 8; one, 3; one, 2; and four, 1 year. None of these have shown any evidence of spread of tumor.

DISCUSSION

A critical analysis of these comparative results may suggest that the cases selected for radical removal may have been very early or very small tumors. Also, because no metastases could be demonstrated even if the tumors were large, it may have been most likely that these were among the less malignant types. Also no effort has been made to separate these tumors at this time into the various types, except that we have noted the benign tumors among the living in cases with inguinal removal, and have not listed among the radical cases any patient in whom it was apparent that the tumor was not malignant after removal. Three of the patients among those who submitted to operation had had previous needling of the scrotum done elsewhere for aspiration of a supposed hydrocele. All of these reported that blood was obtained at the aspiration. Six out of the 20 patients alive showed, microscopically, cells in the lymph nodes, diagnosed as malignant tumor cells. These definitely could not have been removed by an inguinal incision. It is also possible that the pathologist may have missed tumor cells in the lymphatics in other cases. The selection of cases for radical operation was not upon size or duration of the tumor. Among the 43 patients who had inguinal removal were some who were of short history duration and small tumor mass. The cases selected for radical procedure were those in which no metastases could be shown. The selection for inguinal incision was determined by the member of the staff responsible for the case, and largely were those with definite or suspicious shadows of metastases. Also it was believed that an accurate pathological diagnosis may have been an aid to the radiotherapeutist.

It is difficult to compare too closely the value of therapeutic results in testicular tumors, because they vary so much in their growth and their dissemination. The sensitivity of the various tumors to radiotherapy differs. The work of Dean and others based upon experience and end results has fairly well established the

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Four patients were operated on through the scrotum, and then the diagnosis discovered. These cases had transilluminating hydroceles and on exposure of the testis, the tumor was found. All then had inguinal removal of the cord and the scrotal contents. Immediately subsequent to the operation the patients were subjected to x-ray therapy. Two patients died a year after the operation. One was followed for a year without demonstrable metastases, and then lost to follow-up. One was followed for 2 years without change.

INGUINAL INCISION BUT NO X-RAY THERAPY

Nine patients were so treated. X-ray therapy was either refused by the patient or considered unnecessary by the surgeon in the adult teratomas and the interstitial cell tumor. One patient who had a malignant tumor died in 1 year. One patient was followed for 3 years, one for 5, one for 6, and one for 16 years. Among these 5 cases of malignant tumor, there was 1 death and 4 survived over 3 years. One of these patients was a severe tabetic in whom the tumor was discovered in correcting a large hydrocele that extended into the inguinal canal. Of the 4 "benign" tumors, one, an interstitial tumor, is alive and well 4 years later and the 3 adult teratomas have been followed for 4, 7 and 20 years.

INGUINAL INCISION FOLLOWED BY X-RAY THERAPY

Forty-three patients were treated. Of these, 23 are known to be dead. Eighteen died in 1 year, 4 in 2 years and 1 in 4 years. These patients often had some metastases shown at the time of orchiectomy, and the poorest prognosis. The remaining twenty may or may not have had metastases demonstrated or suspected at the time of operation. One has been followed for 18 years, one for 17, two for 15, one for 12, one for 9, one for 8, one for 7, one for 6, one for 5, three for 4, one for 3, and 3 for 2 years. In this group we had the largest number of cases that were lost to follow-up during the war years

RADICAL REMOVAL BUT NO X-RAY THERAPY

Three patients refused x-ray therapy following radical removal. One has been followed 20 years, one for 8 and one for 7 years, all free from apparent metastases or recurrence.

RADICAL REMOVAL FOLLOWED BY X-RAY THERAPY

Twenty-six patients were treated in this manner. Of these, 6 are dead. Four of these done in the early part of the study had metastases present in the secondary areas at the time of the operation. All four died in 1 year from metastases. One patient done later with no evident metastases in the secondary lymphatics died in 2 years with diffuse metastases through the secondary lymphatics. One patient died in 14 years with metastases in the secondary lymphatics. The remaining 20 patients have been followed practically to date and the data are most accurate. Two are alive 20 years; one, 19; two, 18; one, 17; two, 13; three, 12; one, 11, one, 10; one, 8; one, 3; one, 2; and four, 1 year. None of these have shown any evidence of spread of tumor.

DISCUSSION

A critical analysis of these comparative results may suggest that the cases selected for radical removal may have been very early or very small tumors. Also, because no metastases could be demonstrated even if the tumors were large, it may have been most likely that these were among the less malignant types. Also no effort has been made to separate these tumors at this time into the various types, except that we have noted the benign tumors among the living in cases with inguinal removal, and have not listed among the radical cases any patient in whom it was apparent that the tumor was not malignant after removal. Three of the patients among those who submitted to operation had had previous needling of the scrotum done elsewhere for aspiration of a supposed hydrocele. All of these reported that blood was obtained at the aspiration. Six out of the 20 patients alive showed, microscopically, cells in the lymph nodes, diagnosed as malignant tumor cells. These definitely could not have been removed by an inguinal incision. It is also possible that the pathologist may have missed tumor cells in the lymphatics in other cases. The selection of cases for radical operation was not upon size or duration of the tumor. Among the 43 patients who had inguinal removal were some who were of short history duration and small tumor mass. The cases selected for radical procedure were those in which no metastases could be shown. The selection for inguinal incision was determined by the member of the staff responsible for the case, and largely were those with definite or suspicious shadows of metastases. Also it was believed that an accurate pathological diagnosis may have been an aid to the radiotherapeutist.

It is difficult to compare too closely the value of therapeutic results in testicular tumors, because they vary so much in their growth and their dissemination. The sensitivity of the various tumors to radiotherapy differs. The work of Dean and others based upon experience and end results has fairly well established the radiological techniques. From Dean's statistics it appears that for all types of testicular tumors his survival rate for patients who had received preoperative radiation was higher than for patients who received radiation only after orchiectomy. Other reporters oppose preoperative radiation. None of the cases presented in this report received preoperative radiation. It is fairly well agreed by workers in the field that roentgen therapy is a primary importance in the management of seminoma of the testis and has profoundly altered the prognosis; also, that often it apparently fails to prevent the march of the disease. The results apparently are far different in teratocarcinomas or other tumors which have shown a variable resistance to radiotherapy. Recently more massive doses over longer periods have been suggested and used for teratocarcinomas. Complicating damage to the stomach, intestines, liver and kidneys have occurred, but with the known fatal termination of these tumors when they have metastasized, the risk of visceral damage may be justified.

In our experience radical surgery was of no greater hazard than that of inguinal removal. There were no operative mortalities in either type of removal. It is hard to understand the constant recurrence in discussion upon the subject of the "high mortality with radical removal" which seems to be quoted down from the dim past. Under modern surgical techniques the mortality should be the same in inguinal removal as it has been shown to be in our hands. In addition there were practically no complications and all made good surgical recoveries. The healing of the larger incisions was rapid and there have been no hernias or weaknesses in any of the cicatrices. Again it is stressed in this report that we operatively removed both seminomas and teratocarcinomas by the radical procedure. We insisted upon all the seminomas receiving in addition postoperative radiotherapy. We also advised and gave radiotherapy to teratomas. The 3 patients who refused radiotherapy were cases of teratoma

SUMMARY

From a study made of 93 cases of malignant tumors of the testicle in order to evaluate the radical removal of these tumors, it appears that the procedure is of no greater risk, produces no complicating deformity and gives a greater freedom from recurrences when used in a selected group of cases, than other forms of therapy in the same clinic for the same original pathological condition. Although the figures are small, radical surgery appears to yield the same favorable results without radiotherapy. The technique apparently is especially favorable in those cases in which it was combined with postoperative radiotherapy.

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LEIOMYOMA OF THE SPERMATIC CORD WITH THE REPORT OF A CASE

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Tumors of the spermatic cord are infrequent. In a review of the literature in 1939, Schulte, McDonald and Priestley[1] were able to find only 247 cases. Benign tumors were the most common, accounting for 71 per cent of the total. The benign neoplasms included lipomas, fibromas, leiomyomas, dermoids, teratomas, lymphangiomas, hemangiomas, myxomas, myxofibromas, neurofibromas, and cystadenomas. There were 90 reported cases of lipomas, 34 of fibromas, and 14 of dermoids, with a scattering of the others. Malignant tumors were reported in 65 cases, of which 15 were called fibrosarcomas and 39 sarcomas. Other rare malignant neoplasms found were leiomyosarcomas, rhabdomyosarcomas, reticulum cell sarcomas, lymphosarcomas, myxochondrosarcomas, and carcinomas.

Leiomyoma of the spermatic cord is a rare disease, only nine instances having been recorded in the literature.[2–7] Five of these were described as leiomyomas and the other four as myomas. The rarity of this tumor arising in the spermatic cord has prompted this report.

CASE REPORT

A 72-year old white man had enjoyed excellent health until 7 years before admission to this hospital, when he noted a mass in the left inguinal region just superior to the scrotum. A clinical diagnosis of inguinal hernia was made and a herniorrhaphy was performed. At operation a mass was encountered in this region and was removed. It was firm, smooth, and circumscribed. No mention was made of its relationship to surrounding structures, particularly the spermatic cord. Microscopically (fig. 1), it revealed a loose fibrous structure with a myxomatous component and some fat cells. The pathological diagnosis was myxolipofibroma.

The patient did quite well until 2 years later, at which time he complained of urinary frequency, nocturia and dysuria. Examination revealed normal external genitalia with no evidence of a mass in the scrotum or inguinal regions. A 24F sound was passed without any difficulty. The prostate was smooth, nontender, and normal in consistency. A smear of the prostatic secretion revealed only an occasional white blood corpuscle. There was an 8 ounce residual urine. Cystoscopy revealed trilobar hyperplasia and a coarsely trabeculated bladder mucosa. A transurethral prostatic resection was done a month later under caudal anesthesia.

Aided by the Louis M. Monheimer Memorial Fund

[1] Schulte, T. L., McDonald, J. R. and Priestley, J. T.: J.A.M.A., 112: 2405, 1939.

[2] Trélat: J. de méd. et de chir. prat., p. 259, 1880.

[3] Patel, M. and Chalier, A.: Rev. de chir., 39: 119, 354, 603, 798, 942, 1909; 40: 167, 306, 1909.

[4] Schuessler, H.: Deutsch. Ztschr. f. Chir., 135: 268, 1916.

[5] Lapeyre, J. L., and O'Daly, J. A.: Ann. d'anat. path., 14: 70, 1937.

[6] McCook, W. M.: Am. J. Surg., 56: 499, 1942.

[7] Atlas of Genitourinary Pathology, Army Registry of Pathology, p. 182, 1946.

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hematoxylin and eosin stains revealed that the mass was composed of interlacing bundles of smooth muscle fibers, some cut longitudinally and some transversely. A small amount of fibrous tissue was also present. The diagnosis was leiomyoma of the spermatic cord.

The patient had an uneventful postoperative course and was shortly discharged from the hospital.

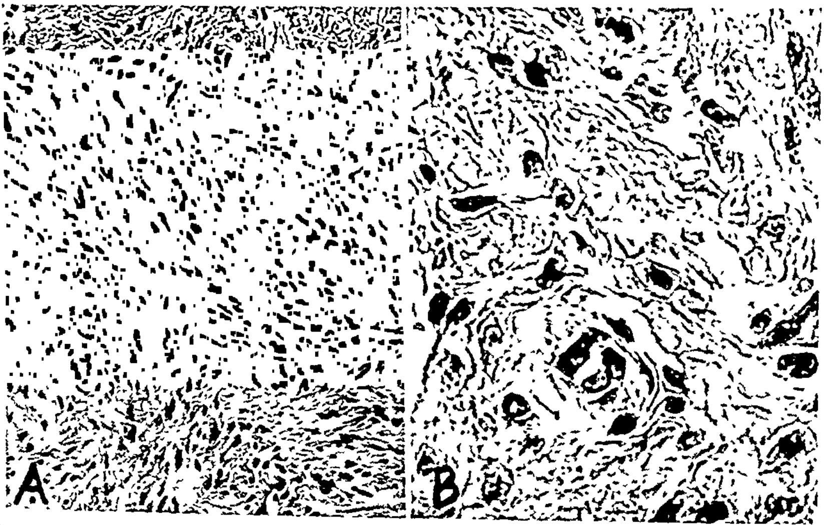

FIG. 3. Photomicrographs illustrating interlacing bundles of smooth muscle in leiomyoma. Hematoxylin and eosin (*A*, X 190; *B*, X 680).

DISCUSSION

As pointed out in the introduction, leiomyoma appears to be one of the rarest of a small group of tumors arising from the structures of the spermatic cord. Trélat[2] reported one instance in an infant. Four cases were collected by Patel and Chalier,[3] and other isolated cases[4–7] have also appeared in the literature.

Portalier,[8] in a review of the subject, stated that in most instances these growths arise from the smooth muscle of the cremasteric internus. It is also thought by others that they may originate from the smooth muscle in the vas deferens.[7] Whether or not they may originate from other smooth muscle in the cord, such as that in the vessel walls, is not known. Stout[9] believes this may be the source of origin of leiomyomas in many sites, although he does not specifically mention this with respect to the spermatic cord. In most cases the leiomyomas were found in the region of the junction of the vas deferens and epididymis, and were generally adherent to both. They usually do not attain the large size of a lipoma, and their consistency is frequently between that of the soft lipoma and hard fibroma.

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[8] Portalier: Contribution à l'étude des leio-myomes du cordon spermatique, Thèse de Lyon, 1908.

[9] Stout, A. P.: Human Cancer. Philadelphia: Lea and Febiger, 1932, pp. 562.

The patient had an uneventful postoperative course. The pathological diagnosis was benign hyperplasia

Four years after the prostatectomy another mass (fig. 2) was felt in the lower left inguinal region, which was firm, smooth, well circumscribed, and nontender. No impulse was detected on coughing and the external ring was snug. The mass did not transilluminate light, and it was dull to percussion. The patient postponed surgery until 6 months later when it was noted that the tumor had increased about 1½ times in size. At operation the mass was attached to the spermatic cord and was carefully dissected free It was rubbery in consistency, light tan in color, had a smooth, encapsulated surface, and measured 4.5 by 3 5 by 3 cm. The cut surface was composed of interlacing bands and whorls of tan colored fibers. No discrete vessels leading to the tumor were observed, and there were no involved lymph nodes. Microscopic examination (fig. 3) with van Gieson and

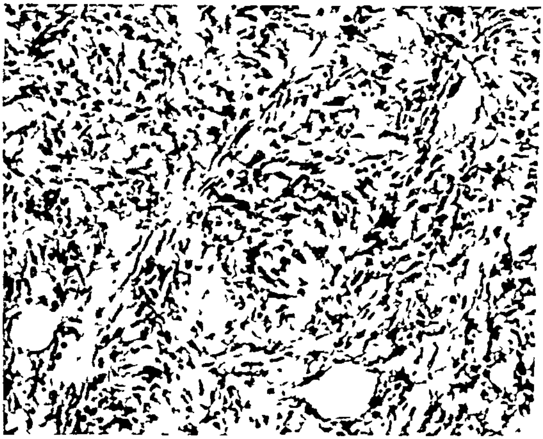

FIG 1 Photomicrograph of myxolipofibroma illustrating myxomatous fibrous tissue with fat component Hematoxylin and eosin (X 190)

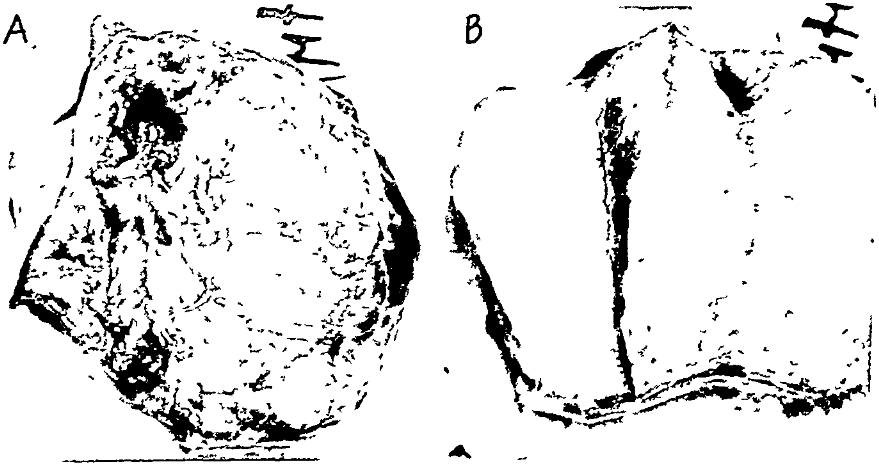

FIG 2 Photographs showing, *A*, external surface and *B*, cut surface of leiomyoma

hematoxylin and eosin stains revealed that the mass was composed of interlacing bundles of smooth muscle fibers, some cut longitudinally and some transversely. A small amount of fibrous tissue was also present. The diagnosis was leiomyoma of the spermatic cord.

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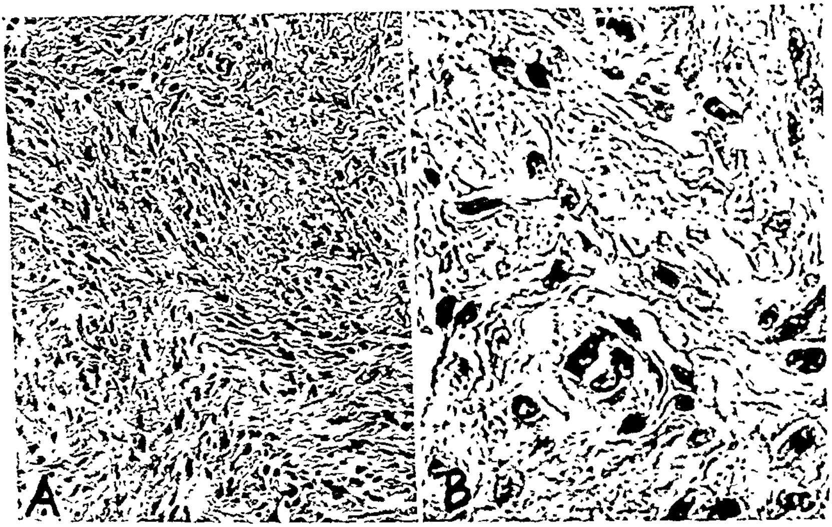

Fig. 3. Photomicrographs illustrating interlacing bundles of smooth muscle in leiomyoma. Hematoxylin and eosin (*A*, X 190; *B*, X 680).

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In our case, the structural element containing smooth muscle from which the leiomyoma arose has not been determined. The previous existence of a tumor in the same local area does not seem to be related to the leiomyoma. The myxolipofibroma showed no microscopic evidence of smooth muscle; and in the sections of the leiomyoma no areas of adipose tissue or myxomatous stroma could be found. Furthermore, since the structure in which the myxolipofibroma originated is not known, it must be assumed that these were independent tumors.

SUMMARY

A case of leiomyoma of the spermatic cord is reported. The rarity of this tumor in this location is pointed out.

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PEDIATRIC UROLOGICAL ADMISSIONS

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What constitutes a pediatric urological service? What may the resident doctor expect to see during his rotation through such a service? In answer to these questions a review of the diagnoses of 1252 individual patients admitted to the Babies Hospital service of the Squier Urological Clinic has been prepared. A 6 year period was covered, from November 1942 to November 1948. Interest in pediatric urology has been heightened recently by the increased emphasis placed upon it by the American Board of Urology. Progress in this field has been limited in the past by the lack of documented clinical material in significant quantities. A preliminary sampling of the admissions to one pediatric urological service is presented here.

This survey did not include re-admissions, as for multiple stage operations or for follow-up. Neither did it include patients who were treated in the outpatient department but not admitted to hospital beds. It does not in any way represent the incidence of these diseases relative to the general population. There were approximately 21,835 admissions to the entire Babies Hospital during a comparable 6 year period, but only an approximate comparison can be drawn here since the total of 21,835 included an unknown number of re-admissions.

All of the patients were under 13 years of age. Each patient has been listed here under only one diagnosis. This has caused some difficulty, as in cases with multiple anomalies, and in cases where two conditions, such as stricture and infection were present. In such cases with multiple diagnosis, only the most fundamental diagnosis was listed.

The patients were first listed in order of the frequency of the various diagnoses (table 1). The cases were next considered from the point of view of the organ involved.

DISORDERS OF THE KIDNEY, KIDNEY PELVIS AND URETER

Hydronephrosis was the principal diagnosis in 94 (7.5 per cent) of the patients. This disorder was found to be due to many different causes. One large group was due to a generalized flaccid dilatation of the ureters and pelves, probably on a neurogenic basis. Other cases of hydronephrosis resulted from strictures at the ureteropelvic junction, strictures of the ureters, ureteroceles and obstructions low in the urinary tract. Several other cases of hydronephrosis resulted from chronic infection of the kidneys. Unlisted hydronephrosis was also present in many of the cases included under horseshoe kidney, pyelonephritis, absence of the abdominal musculature and exstrophy of the bladder.

Pyelonephritis was the major diagnosis in 91 (7.3 per cent) of the patients. The degree of severity was not considered. The majority of these were nonspecific infections but there was one case of tuberculosis of the kidney. Many

TABLE 1. *1252 pediatric urological admission diagnoses listed in order of the frequency of their occurrence (no readmissions included)*

ORDER OF FREQUENCY			NUMBER OF CASES	PER CENT
1	Phimosis or redundant prepuce		230	18.4
2	Cryptorchidism			
	Unilateral	117		
	Bilateral	28		
		145	145	11.5
3	"No urological disease found"		100	8.0
4	Enuresis and frequency		99	7.9
5	Hydronephrosis		94	7.5
6	Pyelonephritis			
	Nonspecific	90		
	Tuberculous	1		
		91	91	7.3
7	Hypospadias		77	6.1
8	Hydrocele		65	5.2
9	Stricture of the urethra		62	4.9
10	Cystitis		35	2.8
11	Sexual and adrenal abnormalities			
	Pseudohermaphroditism	21		
	Hypergenitalism	6		
	Froelich's	4		
	Pheochromocytoma	3		
	Sympathicoblastoma	1		
	True hermaphroditism	2		
	Hypogenitalism	2		
	Hirsutism	1		
	Gynecomastia	1		
	Interstitial cell tumor	1		
	Masculinizing adrenal tumor	1		
		43	43	3.4
12	Congenital deformity of the kidney		39	3.1
13	Neurogenic bladder		32	2.5
14	Hernia		22	1.8
15	Other lesions involving the penis, testes and prostate		21	1.7
16	Injuries to the genito-urinary tract		17	1.4
17	Fistulas, urethrovaginal and urethrorectal, plus imperforate septa of anus, urethra and vagina		16	1.3
18	Exstrophy of the bladder		16	1.3
19	Wilms tumor		10	0.79
20	Vaginitis and urethritis		9	0.71
21	Patent urachus		6	
22	Epispadias		5	
23	Sulfa drug reactions involving the kidneys		5	
24	Hemophilia with hematuria		5	
25	Absent abdominal musculature with hydronephrosis		4	
26	Bladder papilloma		1	
27	Pelvic abscess		1	
28	Ovarian cyst		1	2.4
	Total		1252	100

additional unlisted cases of pyelonephritis were seen as complications of obstructive lesions. There were three cases of renal rickets among the 1252 patients.

Supernumerary ureters and kidney pelves were found in 1.3 per cent of the patients, and of these there were 6 patients (0.5 per cent) who had an ectopic ureteral orifice somewhere in the vulva. One patient had an ectopic kidney, 1 a hypoplastic kidney, 2 had a congenitally absent kidney and 1 had nephroptosis. Two patients had albuminuria of undiagnosed cause, 1 patient had a perinephric abscess and 1 patient had 4 separate kidney pelves and ureters. Malrotation of the kidney was present in 3 patients. Horseshoe kidneys were found in 3 out of the 1252 patients, and congenitally cystic kidneys in 2. Five patients had reactions to sulfa drugs; 2 with moderate oliguria, 1 with hematuria and 2 with anuria due to sulfa drugs. Injury to the kidney occurred in 9 instances. Four patients had absence of the abdominal musculature complicated by severe hydronephrosis and hydro-ureter. Twelve patients (1 per cent) had Wilms' tumors.

SEXUAL, VESICAL AND GENITAL DISORDERS

Forty-three (3.4 per cent) of the patients had sexual abnormalities. Twenty-one (1.7 per cent) of the total were investigated for pseudohermaphroditism, 2 others were true hermaphrodites, 6 more showed hypertrophy of the genitalia, 4 were cases of Froelich's syndrome, 1 patient had hirsutism, 1 had gynecomastia and 2 patients had hypogenitalism. One patient had an ovarian cyst. There was one interstitial cell tumor of the testis. There were 3 pheochromocytomas. One sympathicoblastoma was admitted on this service. The high incidence of adrenal disorders was due to Dr. George Cahill's particular interest in this subject.

Seventy-seven (6.1 per cent) patients were admitted for repair of hypospadias. A few additional unlisted cases of hypospadias and cryptorchidism were found, of course, among those children with a diagnosis of pseudo or true hermaphroditism.

Sixteen patients (1.3 per cent) had exstrophy of the bladder, several with unlisted hernias and cryptorchidism in addition. Six patients had epispadias. One hundred and forty-five patients (11.6 per cent) had cryptorchidism, of which 117 (9.4 per cent) were unilateral, and 28 (2.2 per cent) were bilateral. Twenty-two patients (1.8 per cent) presented hernias. Seven patients had urethrorectal fistulas, 1 patient had a rectovaginal fistula, 5 patients had imperforate anus, 2 patients had imperforate vagina and 1 patient had 2 vaginas. Seven patients showed vaginitis.

Thirty-two patients (2.5 per cent) were found to have neurogenic bladders. Some of these were complicated with unlisted hydro-ureters and hydronephroses, as well as cystitis and pyelonephritis. Where the major diagnosis was neurogenic bladder and the diagnosis was definite, they were listed under neurogenic bladder only. Cystitis due to routine organisms occurred in 31 cases. One patient had a protozoan cystitis, 1 had interstitial cystitis, 1 had severe hemorrhagic cystitis, 1 had a foreign body in the bladder, 6 had patent urachus and 1 had a bladder tumor. Five patients had hemophilia and hematuria. Three patients had undiagnosed urinary frequency. Enuresis was the only diagnosis in 99 patients (7.9 per cent). Additional patients had enuresis, however, who were circumcized and therefore included under the listing of redundant prepuce. There were 62 (4.9 per cent) with urethral obstruction, of which 51 were strictures of the urethra or urethral meatus, where most occur. Five more were strictures resulting from injury. Three of these cases of injury were due to accidents during circumcision elsewhere, at which time the glans penis was inadvertently removed and a stricture of the urethral stump resulted. Five of the 51 cases of urethral stricture were located at the bladder neck. In only 2 of these 1252 cases were well-defined valves found in the posterior urethra. Miscellaneous ailments involving the penis included 3 cases of injury, 5 cases of infection of the skin of the penis, 3 cases of sebaceous cyst, 2 cases of hematoma, 1 case of absence of the penis and 1 case of penile dermatitis from poison ivy. There was 1 birth injury to the urethra.

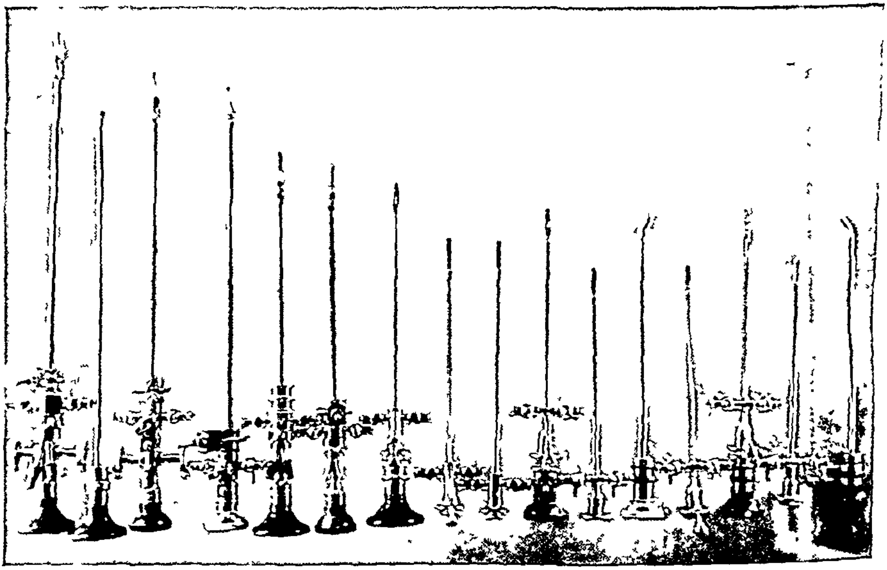

FIG. 1. Infant cystoscopes of various specifications in use at the Squier Urological Clinic

The testis was involved in 5 cases with torsion of the testis; 1 case with torsion of the hydatid of Morgagni. The testis was injured in 1 patient and 1 patient came in with orchitis. There was injury to the scrotum in 1 case, prostatitis in 1 case and a large, fleshy appendage to the perineum in 1 case. A redundant or phimotic prepuce was removed from 230 (18.4 per cent) of the patients, many of whom were in the hospital because of enuresis, or for investigation of some other ailment such as balanitis. One hundred cases showed no evidence of urological disease after thorough work-up. Those patients had been admitted for various reasons, some because of undiagnosed abdominal pains, obscure fevers or other diagnostic problems.

TYPE OF LESION

Finally, the lesions were classified as to type:—1) those due to congenital anomalies, 34.2 per cent; 2) those due to infections of the genito-urinary tract 11.0 per cent; 3) those with tumors of the genito-urinary tract, including adrenal tumors, 1.4 per cent; 4) those with miscellaneous diagnoses including redundant prepuce, enuresis and "no disease found", 53.4 per cent.

The Babies Hospital service of the Squier Urological Clinic has been developed and equipped at the Columbia-Presbyterian Medical Center over the past 12 years. One floor of the Babies Hospital is devoted to pediatric urology, and is continuous with the Medical Center floor occupied by the urological x-ray, cystoscopic department, wards and laboratories of the Squier Urological Clinic. The availability of this service has made easier the early diagnosis of organic pathology in the genito-urinary tract.

Two attending urologists from the Squier Clinic supervise all diagnostic and surgical procedures and an attending pediatrician supervises all pediatric work-up and treatment. One Squier Clinic resident, in an advanced stage of his residency, is assigned to this service specifically and spends at least 6 months on the service. One pediatric assistant resident, supervised by the pediatric chief resident, is assigned here and does a complete medical work-up, regulates the diet and handles all medical problems peculiar to each child. A special permanent nursing staff, with a particular appreciation for the idiosyncrasies of urological devices, is assigned to the service.

Observation cystoscopes of 8F diameter are used. Butterfield and McCarthy catheterizing cystoscopes of both 12 and 15F diameter are used, and for very large children, 16F Brown and Buerger cystoscopes are available (fig. 1). A McCarthy infant resectoscope is used for bladder neck obstructions. A supply of especially small woven catheters, bougies and filiforms is kept sterile and under refrigeration. It is apparent to those who have worked on this service that a child's genito-urinary tract is not just a miniature adult tract and cannot be handled as such. The opportunities for constructive research in this field are manifold. It is hoped that the experience gained through a large number of admissions to active services devoted entirely to pediatric urology will make it possible to solve the many therapeutic problems now before us.

SUMMARY

A sampling from the experience of one pediatric urological service has been presented. One thousand, two hundred and fifty-two individual admission diagnoses were catalogued. The largest and most significant single group was made up of patients with congenital anomalies (34.2 per cent). The second largest group was made up of those with infections (11 per cent). Overlapping of the various groups was frequently found. A more comprehensive analysis of all pediatric urological admissions to this service will be reported periodically.

Acknowledgement is here made of the courtesy of Drs. Cahill, Fish, Robinson, Hazzard, Melicow, Yeaw, Sullivan and Seidel in permitting the inclusion of some of their patients in these series.

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TRICHOMONAS INFESTATION IN THE MALE: A PRELIMINARY REPORT

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Investigation of trichomonas infestation in male patients was undertaken at the Detroit Receiving Hospital outpatient clinic. This study was inspired by the noticeable frequency with which trichomonads were found in the voided urine specimens submitted for routine and microscopic analysis.

In recent years an increasing awareness of this condition by the practitioner has resulted in additional statistical information which would lead one to surmise that the incidence of this disease in the male is not as rare as was formerly believed.

The reported incidence of this condition has varied widely with different investigators. L. G. Stuhler reported the finding of 16 cases of trichomonads in 32,000 prostatic secretions examined at the Mayo Clinic. Nitschke reported an incidence of 12.5 per cent of 40 cases of nonspecific urethritis having trichomonads in the urethral secretions. Liston and Lees in England found an incidence of 16 cases of trichomonads in the urine in a series of 400 male urine specimens examined. Riba described 9 cases of prostatovesiculitis with trichomonads present in 3000 prostatic secretions and suspected this to be a lower incidence than was actually the case. The literature thus far submitted on trichomonas infestations in the male has been in no way uniform, either as to the type of examination or the material examined.

We believe that this disease can be more readily detected through the examination of freshly voided urine as has been suggested by other investigators; namely, Strain and Roth, as we have found urine sediments positive for trichomonads in cases in which we were unable to demonstrate the organisms in either repeated urethral or prostatic secretions. We do not, however, infer that the organisms are not primarily inhabitants of the urethra.

All material was examined during this investigation within 5 to 10 minutes after being voided. Sterilized urine containers and centrifuge tubes were utilized to exclude false positives. Microscopic examination by both direct and indirect lighting was employed to identify these organisms, but with indifferent advantage. The phase microscope was utilized on some cases, but found to be of no particular value. Various types of protozoal stains and supravital stains were employed as well as gram and methylene blue stains, but all proved unsatisfactory and impractical.

During a period of 4 months a total of 2305 urine specimens were examined in the outpatient clinic of the Detroit Receiving Hospital which represented the freshly voided specimens of all types of clinic patients. Of this number, 1338 were the urines of female patients and 967 were urines of male patients. A further breakdown showed that 68 per cent of this total were colored and 32

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per cent white. The 1338 voided urine specimens from female patients showed 162 containing trichomonads, for an incidence of 12.1 per cent. The 967 voided urine specimens from male patients showed 42 containing trichomonads, giving an overall percentage for males of 4.3 and probably approximating a population incidence for this social and economic level. The incidence of trichomonads in the urines of female patients as compared to male patients was approximately 3 to 1 (table 1).

Only two of the 42 male patients in which trichomonads were demonstrated in the urine were currently attending the urology clinic for relief of symptoms referable to the genito-urinary tract. It was possible to contact 15 additional cases for further study, and these reported to the clinic by special invitation.

The age incidence of the 17 patients studied ranged from 30 to 73 years with an average of 49. There were 38 Negro and 4 white patients, which gave a racial incidence of 5.7 per cent Negro and 1.3 per cent white patients showing trichomonads in the urine.

TABLE 1. *Incidence of trichomonads in 2305 voided urines*

	TOTAL URINES	POSITIVE FOR TRICHOMONADS	INCIDENCE
			%
Females	1338	162	12.1
Males	967	42	4.3

TABLE 2 *Symptoms and signs*

	CASES	PER CENT
Symptoms		
Nocturia (2 or more)	12	71
Urgency	10	59
Dysuria	7	41
Itching sensation	5	29
Deep pelvic pain	5	29
Signs		
Urethral discharge	12	71
Stricture	6	35

The predominant symptoms of the 17 studied cases were: nocturia, 2 or more times, in 12 cases; urgency in 10; dysuria in 7; itching sensations along the course of the urethra and about the meatus in 5 cases; and deep pelvic pain in 5 cases.

The physical finding of urethral discharge, stated to be particularly noticeable on arising, was present in 12 cases. Evidence of urethral stricture was noted in 6 patients (table 2).

Laboratory studies revealed pyuria in 14 cases. Bacteria were present in the centrifuged urine specimens in 12 patients and were for the most part staphylococci, diphtheroids, and M. epidermis. Microscopic examination of the thin milky urethral discharge present in the 12 cases revealed active trichomonads in 8. The urethral secretions contained both epithelial cells and white cells in all 12 instances. Prostatic secretions were obtained and studied from all 17 cases. Trichomonads were found in 12 patients. It is interesting to note that the finding of trichomonads in the prostatic secretion did not coincide in every instance with the finding of trichomonads in the urethral secretion. White cells were present in the prostatic secretion in all 17 cases as was expected, and varied from 5 to 10 white cells/high powered field to innumerable white cells. There appeared to be, however, no direct relationship between the finding of trichomonads in the prostatic secretion and the number of white cells present. Bacteria were present in 15 instances, and more than an occasional epithelial cell was noted in the prostatic secretion in 11 cases (table 3).

Two of these patients were admitted to the hospital for urethroscopic study as well as cystoscopy and retrograde pyelography. Examination of the bladder in these two patients disclosed no evidence of unusual pathological change. The urine specimens taken from the bladder as well as separate kidney urine specimens failed in each case to show trichomonads. The prostatic urethra as well as anterior urethra in each case showed only mild inflammatory changes.

TABLE 3. *Laboratory studies*

	CASES	PER CENT
Pyuria	14	82
Bacteruria	12	71
Trichomonads urethral	8	47
Trichomonads prostatic	12	71
Bacteria, prostatic	15	88

A review of the literature discloses a strikingly wide variety of therapeutic agents employed in attempts to eradicate this infestation in the male, and is evidence of a lack of a specific treatment. In 8 cases either one or more of the following agents were employed; penicillin, sulfonamides, calcium mandelate, and chloromycetin. In no instance was a trichomonad-free secretion obtained, either from the urethra or prostate. Six of these patients in whom trichomonads were present not only in the urine, but in the urethral and prostatic secretions as well, were then treated orally with a saturated solution of potassium iodide. The centrifuged urine sediments, urethral and prostatic secretions were thereafter studied at weekly intervals. Patients were maintained on this medication for an average of 2 weeks. Three of the 6 cases so treated showed a persistence of active trichomonads in the urinary sediment, urethral and prostatic secretions, whereas in 3 others it was impossible to find the organisms for a period of as long as 4 weeks after the cessation of treatment. No additional therapy such as urethral irrigations, prostatic massage or passage of sounds was utilized on these patients. In view of the rather well established fact that these organisms may enter into a resting or encysted stage for as long as 2 or more months and during which time identification of the organism may be exceedingly difficult or impossible, we do not offer this therapy as definitive.

CONCLUSIONS

Trichomonas infestation of the male genito-urinary tract is not rare, as shown by an overall incidence of 4.3 per cent of clinic patients.

Microscopic examination of the sediment of freshly voided urine is the most reliable method of detection of this condition in the male.

Negroes showed trichomonas infestation approximately 5 times as frequently as white patients.

The signs and symptoms of this infestation are often considered insignificant by the patient and accepted with little or no concern.

The predominant symptoms are nocturia, urgency and dysuria, itching along the course of the urethra and about the meatus, and deep pelvic pain.

The physical findings of a thin milky urethral discharge and of evidence of urethral stricture were noted most frequently in these patients.

Laboratory studies revealed pyuria and bacteriuria as a common finding. Active trichomonads were present in 8 of 12 urethral secretions, and 12 of 17 prostatic secretions. The finding of trichomonads in both the urethral and prostatic secretions does not necessarily co-exist in each case.

There appears to be no direct relationship between the finding of trichomonads in the prostatic secretion and the number of white cells present.

The most encouraging therapeutic results obtained were with potassium iodide. Further investigation along this line and the study of other iodide preparations are merited.

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REFERENCES

Baumeister, C. and Hollinger, N.: Trichomonas infection of the male genito-urinary tract. Arch. Surg., **43:** 433, 1941.

Bisher, J. W.: Vesical infection with trichomonas vaginalis. J. A. M. A., **92:** 2098, 1929.

Drummond, A. C.: Trichomonas infestation of the prostate gland. Am. J. Surg., **31:** 98, 1936.

Feo, L. G.: Incidence and significance of trichomonas vaginalis infestation in the male. Am. J. Tropical Med., **24:** 195, 1944.

Liston, W. G. and Lees, R.: Trichomonas vaginalis infestation in male subjects. Brit. J. of V. D., **16:** 34–35, 1940.

Lydon, F. L.: Trichomonas vaginalis infestation in the male. Brit. Med. J., p. 384, Sept. 22, 1945.

MacDonald, E. and Tatum, Al.: In vitro action of various chemical agents on trichomonas hominis, trichomonas vaginalis, and trichomonas foetus. J. Immun., **59:** 301, 1948.

Nitschke, P. H.: Trichomonas vaginalis infestation in the male. J. A. M. A., **108:** 12–14, 1936.

Pomeroy, E. S.: Seventh venereal disease? Urol. & Cutan. Rev., **52:** 72–73, 1948.

Riba, L. W. and Harrison, R. M.: Strictures of the male urethra and trichomoniasis vaginalis. Surg., Gynec. & Obst., **71:** 369, 370, 1940.

Riba, L. W.: Trichomonas urethritis. J. A. M. A., **96:** 2100, 1931.

Strain, R. E.: Trichomonas in the male. J. Urol., **54:** 483, 1945.

Stuhler, L. G.: Trichomonas vaginalis infestation of the prostate gland. Proc. Staff Meet, Mayo Clinic, **8:** 221, 1933.

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MANSON'S SCHISTOSOMIASIS WITH UNILATERAL INVOLVEMENT OF KIDNEY

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Schistosomiasis is a parasitic disease caused by blood flukes, three species of which are of clinical importance. Man is parasitized by Schistosoma haematobium, S. japonicum, and S. mansoni, which are responsible, respectively, for the vesical or urinary, the Asiatic, and the mansonic forms. The latter two primarily affect the large intestine and the liver.

The urologists practicing in Egypt have been mainly concerned with urinary schistosomiasis due to S. haematobium, since there is no record in the literature of extensive invasion of the urinary tract by the other two parasites. However, eggs have been found in the urine or deposited in the bladder, testicles, and prostate in a few cases.

We are mainly concerned here with Manson's schistosomiasis. This disease has a wide geographical distribution, being found in many parts of Africa, Madagascar, the northern part of South America, and a few islands of the Antilles, including Puerto Rico where only the mansonic variety is found as in the rest of America. On this island, in the municipalities of Caguas, Jayuya, Adjuntas, Utuado, Aibonito, Cayey, and Rio Piedras, 20 to 40 per cent of the population is probably infected, although most cases are not severe.

Even in nonendemic municipalities, like San Juan, a large number of individuals are suffering from schistosomiasis because of shifting of the population from infected areas. Among autopsies performed in the City of San Juan, Koppisch has found an incidence of 14.6 per cent.[1]

The Schistosoma mansoni are slender parasites, 1 to 2.5 cm. long and 1.5 to 3 mm. broad, whose usual habitat is the portal veins and intestinal tributaries. The male worm possesses a trough or gynecophoral canal where the female is held during copulation.

Man contracts the disease while working, swimming, or wading in bodies of soft water. These bodies of water contain a mollusc (Australorbis glabratus) that serves as intermediate host and which is infected by miracidia hatched from ova passed with the feces of infected people. Three or four weeks after having been infected, the snails begin to shed thousands of free-swimming, fork-tailed cercariae which are the form of the parasite infective to man.

The cercariae penetrate the skin or mucous membranes and enter either the veins or lymphatics in the derma or submucosa, then reaching the right side of the heart and passing through the pulmonary circulation into the arterial blood, in which they are distributed to all organs and tissues. Since their course is strictly intravascular, only those parasites reaching the abdominal organs whose blood drains into the portal veins, are able to mature. The young parasites accumu-

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[1] Koppisch, E.: Manson's schistosomiasis. J. A. M. A., **121**: 936–942, 1943.

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late in intrahepatic portal veins, wherein they reach maturity between five and six weeks after invasion of the human host. After reaching adulthood, the worms travel against the blood current and copulate in branches of the inferior mesenteric and colic veins, as well as in the inferior hemorrhoidal venous plexus, which constitute their regular habitat.

After fecundation, the worms separate, the female entering venules that fit her snugly in the wall of the rectum and, in diminishing numbers, at higher levels. Most of the ova are deposited within the venules just above or just below the muscularis mucosae.

The actual mechanism whereby ova pass into the lumen, thus to reach the outside with the feces, for completion of the parasite's life cycle, has never been demonstrated. Kohlschütter and Koppisch[2] investigated this matter a few years ago without being able to settle it. They found, however, that when ova touch upon the endothelial lining of the venules, the endothelial cells quickly extend over the ovum, isolating it from the circulation, and the pseudotubercle then develops about such ova. Oviposition produces irritation, with edema and eosinophilic and round cell infiltration. Small superficial erosions of the mucosa then develop.

The overdistention of superficial mucosal capillaries, produced by the blocking of venules by the ovipositing worms, leads to rupture of some of these capillaries; others probably rupture at the base of the mucosal erosions. Presumably, it is through these points of rupture that some ova manage to escape into the intestinal lumen.

Not all of the eggs are entrapped where laid or pass into the lumen. A good many of them, when the female worm withdraws from the venule after oviposition, are swept with the blood current to intrahepatic portal branches, where they block the smaller veins in the larger portal spaces. The result of this is the formation of pseudotubercles about them, the infiltration of portal spaces with eosinophils, lymphocytes, plasma cells, and monocytes, and the formation of a progressive fibrosis of the portal spaces. After 10 or 15 years, the hepatic affection results in a clinical picture of cirrhosis, with splenomegaly, gastro-esophageal varices, ascites, and anemia. Sometimes the picture is that of Banti's disease, and, at this stage, the only clue to the diagnosis may be a history of residence or sojourn in an endemic focus; a history of exposure to infested waters, which is particularly suggestive when the individual having felt itching in the exposed parts shortly after coming out of the water, and the finding of eosinophilia. These points are of particular importance for diagnosis, because later in the course of the disease, it may be difficult or impossible to find ova in the stools.

The general clinical picture in Manson's schistosomiasis depends on the severity of the infection. Those exposed to only a few cercariae may never present symptoms; others, somewhat more heavily infected, will have occasional bouts of diarrhea, usually with a little blood visible in the stools, and may complain of transient pain in various parts of the abdomen. The more heavily infected will go for years having episodes of bloody diarrhea and abdominal pain; the liver enlarges and then retracts; there is progressive splenomegaly and, finally, after a number of years, the picture is predominantly that of hepatic cirrhosis. According to Koppisch,[3] in Puerto Rico death is due in one third of the fatal cases to hematemesis from rupture of esophageal varices; in another third, to cachexia due to the cirrhosis, and in the remainder, to complications, such as "hyperinfection, partial intestinal obstruction from schistosomal fibrosis of the mesocolon, colloid adenocarcinoma of the cecum, fistula of the ascending colon with formation of a large retroperitoneal abscess, and pulmonary bilharziasis."

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[2] Kohlschütter, E. and Koppisch, E.: On the mode of extrusion of schistosome ova from blood vessels into the tissues. Schweiz. Ztschr. f. Path. u. Bakt., 4: 357, 1941.

Occasionally, the parasites are found in unusual sites, or ova are swept to unusual organs, leading to the so-called aberrant or ectopic lesions. In very heavy infections, worms may oviposit at various levels of the small intestine and in the stomach, pancreas, and spleen, but usually in very small numbers only. They may oviposit in the uterus (including the cervix), fallopian tubes, ovaries, testes, and prostate. A few ova may be found in the urinary bladder. Ova and worms may find their way, perhaps through venous connecting channels between the inferior hemorrhoidal plexus and the inferior vena cava, to the lungs. In that location the worms produce foci of eosinophilic bronchopneumonia, and the ova obstruct arterioles in the form of emboli, which results in the formation of pseudotubercles and of small groups of newly developed capillaries designated by Shaw and Ghareeb[4] as "angiomatoids". These alterations lead to hypertension of the lesser circulation which, in turn, results in right-sided cardiac hypertrophy and a picture of cor pulmonale. Stray ova have also been found in the adrenals, myocardium, and brain.

Müller and Stender reported a case of lumbar myelitis with paraplegia, paralysis of the urinary bladder, and death from urinary tract infection. Curiously enough, schistosomal lesions or ova were not found in any other part of the body in that case. It was first suggested by Koppisch, in 1943,[1] that in this case the worms probably passed from the pelvic vein plexuses to the vertebral plexus, "from where they could reach the tissues of the spinal cord for oviposition. . . ."

As regards the kidney, ova have been occasionally found in microscopic sections, but so far as we have been able to determine from a study of the literature, prolonged hematuria, with obligatory nephrectomy, due to any of the three species of schistosomes pathogenic for man, has not heretofore been reported.

The following case suggests that urologists practicing in endemic areas of schistosomiasis, and those who see patients from such areas, should consider the possibility of schistosomiasis in cases of hematuria of obscure cause, particularly in cases, like our own, known to be infected with the fluke. There have been cases of schistosomal myelitis and encephalitis that have responded to treatment, so that *a priori*, and by analogy, perhaps nephrectomy could be avoided in cases of hematuria due to renal schistosomiasis.

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[3] Koppisch, E.: Studies on schistosoma mansoni in Puerto Rico. VI. Morbid anatomy of the disease as found in Puerto Ricans. Puerto Rico J. Pub. Health and Trop. Med., **16**: 395, 1941.

[4] Shaw, A. F. B. and Ghareeb, A. A.: The pathogenesis of pulmonary schistosomiasis in Egypt, with special reference to Ayerza's Disease. J. Path. and Bact; **46**: 401–424, 1938.

CASE REPORT

P. L. M., Hosp. No. 11993, a 36-year-old mulatto male Puerto Rican, was seen by us for the first time on February 21, 1949 in the Outpatient Department of the University Hospital of the School of Tropical Medicine.

For about one year he had been following treatment in this institution for mansonic schistosomiasis, and splenectomy had been performed on October 13, 1948 by Dr. José Nova Benítez. The postoperative course was uneventful, and the patient was discharged, improved, November 26, 1948.

He was later referred to our service, complaining of massive, persistent, and silent hematuria of 5 months' duration. He stated that for about one year he had been passing, at intermittent intervals, pink or bloody urine. These episodes were of short duration and were not accompanied by colic or by symptoms of bladder irritability. Although blood had been noted in the urine by the medical and surgical staffs prior to splenectomy, it was considered that bleeding from the genito-urinary tract was probably the result of renal congestion due to increased portal hypertension. Prior to splenectomy, he had had three attacks of hematemesis. The patient urinated in a normal fashion, $\frac{3\text{-}4\ \mathrm{ND}}{0\ \mathrm{NN}}$, without hesitancy, urgency, or dribbling. The stream was of normal size and shape; there was mild terminal burning occasionally, but he had never had colicky pain. No calculi, sand, or gravel had been passed in the urine. The family and past histories were noncontributory. The review by systems was essentially negative.

The patient was fairly well-developed and nourished. Temperature 98.6F, pulse 80, respirations 20, blood pressure 130/80. Only positive findings will be noted. The upper abdomen presented a well-healed, surgical, transverse scar. The left lobe of the liver was palpable three finger-breadths beneath the xiphoid process on deep inspiration. The kidneys were not palpable; the urinary bladder was not percussable or tender.

In the left lower quadrant, a hard, slightly tender mass, the size of an orange, and moderately fixed, could be palpated. This mass was suspected to be an ectopic kidney. The external genitalia, prostate, and seminal vesicles were not remarkable. The reflexes were physiological.

The urine was reddish, turbid, and acid; albumin—+; sugar negative; specific gravity 1.018; sediment loaded with red blood cells; no pus or bacteria. Gram stain negative; culture negative. Red blood cells 4,550,000; hemoglobin 84 per cent (12.2 gm.); white blood cells 12,950; stabs 1; PMB 1; PME 25; segmented 32; lymphocytes 41. Phenolsulfonphthalein test 64.63 per cent; bromsulfalein 16.65 per cent; Hanger and thymol 2+; urobilinogen negative; prostate smear negative. Nonprotein nitrogen 32.09; urea nitrogen 16.69; sedimentation rate 22 mm.; Kahn test negative; stools positive for ova of S. mansoni and hookworm; also for Strongyloides stercolaris larvae.

Descending pyelography: In the flat film an enlarged renal shadow was visible.

but no renal shadow could be observed on the left side. To the left of the fifth lumber vertebra, and overlying the inner portion of the iliac crest, a faint, round, smooth shadow was present which corresponded with the mass felt in the left lower quadrant. The right pyelogram was essentially negative, but no dye was seen on the left side.

Cystoscopy was performed on March 21, 1949. The fundus of the bladder, trigone, bladder neck, and posterior urethra, as well as the urethral openings, were not remarkable. Frank blood, however, was spurting from the left ureter. A 5F catheter ascended 16 cm. on the left side. A specimen of bloody urine was collected, which was negative for pus and bacteria. The retrograde pyelogram revealed a nonrotated, ectopic kidney to the left of the fifth lumbar vertebra, and overlying the sacrum and left iliac crest. The calyceal pattern was well preserved. The ureter was short, corresponding with the position of the kidney.

The case was discussed with the medical and surgical services, and a nephrectomy decided upon in view of the severity of the bleeding. A preoperative diagnosis of papilloma, varix, angioma or papillitis was made.

On May 4, 1949, a transperitoneal nephrectomy was performed, under spinal anesthesia, through a transverse incision below the umbilicus. An anomalous blood supply was encountered. A single artery entered the upper pole of the kidney. This artery came from the abdominal aorta. A single artery emerging from the left common iliac artery entered the kidney through the lower pole. From the hilum, and to the left of the pelvis and ureter, a single large vein emerged. This vein ascended upwards and to the left side of the abdomen, instead of to the right side, to enter the vena cava, but we could not trace its end.

The postoperative course was uneventul, and the patient was discharged on May 12, 1949.

Since then he has been seen monthly until one month ago. There has been no recurrence of the hematuria. The urine is entirely normal. Several specimens were examined by centrifugation for schistosome ova, but none were found. The blood chemistry is normal. After the operation, he was given treatment with fuadin, but ova are still present in the stools.

The gross specimen (S.P. 49010) consisted of a kidney including 4 cm. of the ureter. It weighed 150 gm. The capsule stripped off easily, leaving a pinkish-brown, finely granular surface. Instead of the normal kidney shape, it was flattened into the general form of a spleen, with a hilum presenting from one of the flat surfaces near the margin. At opposite poles, 2 accessory arteries were identified. The surface was stippled with petechial hemorrhages. On section the cortex was well demarcated from the medulla and measured 9 mm. in thickness. The glomeruli were visible and congested. Throughout the cortex there were many pinpoint foci of whitish color but having a minute brownish point in the center. The pelvis was not dilated, and the mucosa was smooth, but there were many submucosal hemorrhages. The portion of ureter received was of normal appearance.

Several blocks were obtained, fixed in Zenker's fluid, embedded in paraffin and stained with hematoxylin and eosin. Serial sections were made of two of them.

Eight to nine pseudotubercles were encountered in each section, averaging 1.5 by 1.2 cm. of several blocks. The pseudotubercles were all situated in the cortex and were composed of a central zone of epithelioid cells surrounded by numerous eosinophils, lymphocytes, and plasma cells. A schistosome egg shell could be seen in the center of some of the pseudotubercles and, when present, they were surrounded by foreign body giant cells, but several of the pseudotubercles were cut tangentially and did not include the egg shell. Some of the pseudotubercles were sectioned through the peripheral zone of eosinophilic and round cell infiltration. There were, in addition, isolated foci of dense lymphocytic infiltration situated beneath the capsule and in the interstitial tissues of the cortex. A few adjacent tubules showed atrophy and were slightly dilated and lined by almost flat epithelium. Hyaline casts were present within many of the tubules. The space of Bowman's capsule of most of the glomeruli was distended with coagulated protein. The miracidium within some of the eggs was well preserved. Several blocks that contained no pseudotubercles presented multiple foci of dense infiltration with lymphocytes, and in connection with these areas, in the center or in the periphery of them, there were encountered completely hyalinized glomeruli and several atrophied tubules. The remainder of the renal tissues showed coagulated protein within the tubules and many hyaline casts. An ovum with well preserved embryo was encountered in a vein, a very short distance beneath the cortex. Following several of the foci of round cell infiltration in serial sections showed them to be related to pseudotubercles. In one of the blocks there was encountered a short, longitudinal scar of the cortex, composed of dense fibrous tissue, several atrophied tubules, and one glomerulus that was undergoing hyalinization. When this was studied serially, an egg shell surrounded by a zone of eosinophilic infiltration was encountered. Pseudotubercles that showed no egg shell in the first section were found to contain a shell, with or without an embryo, when followed serially.

COMMENTS

Although we presume, from the unusually large number of pseudotubercles, that the schistosomiasis was responsible for the one-sided hematuria, it is not possible to be entirely certain of this. First, because the affected kidney was ectopic, and the possibility remains that this may have been conducive to congestion, with rupture of capillaries, although no evidence of this was found in the pathologic examination. Second, it is difficult to visualize the hemorrhages as a result of the formation of pseudotubercles. These structures develop about schistosome ova in many organs, and are never accompanied by hemorrhages.

As to the latter point, however, one might argue that the pseudotubercles were all situated in the cortex, which is highly vascular. They were clearly situated in relation to veins in the intertubular or juxtaglomerular connective tissue. From what happens in such organs as the colon and liver, it is to be assumed that female worms penetrated the renal substance for oviposition. The formation of the pseudotubercles frequently led to structural alterations in the glomeruli and groups of tubules, and at the same time, it must have resulted in obstruction of venules, with the consequent congestion, and probable rupture of some of them in their proximal portions.

At operation the renal vein was traced upwards and to the left, but it could not be determined whether it entered the inferior vena cava or some other vein. *We can only surmise that worms passed from the inferior hemorrhoidal plexus* to the inferior vena cava and up the renal vein into the renal substance. There had been slight and occasional hematuria before the splenectomy, but it was not until after operation that the hematuria became severe. The possibility is thus suggested that a portorenal venous shunt may have been accidentally established at the time of operation, and that the worms may have come from the portal venous system.

It is likewise possible that since the affected kidney was ectopic, it may have had an unusual venous supply which may have facilitated the passage of worms to that organ, by a closer relation to pelvic veins or to tributaries of the portal venous system.

SUMMARY

A case of severe hematuria originating in an ectopic left kidney is reported. The kidney contained numerous pseudotubercles of Manson's schistosomiasis. It is suggested that the latter, rather than the ectopic displacement, was responsible for the bleeding. This seems to be the first case reported of extensive renal nvolvement in the course of Manson's schistosomiasis.

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THE CLINICAL INTRAVENOUS NEPHROGRAM: PRELIMINARY REPORT

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The value of a practical clinical method of radiologic demonstration of the renal parenchyma is obvious, and has been sought since 1929 by various investigators. This report is concerned with the description of a simple modification of routine excretory urography that has been found to accomplish this purpose and to provide certain other equally important information as to the anatomic and physiologic status of the upper urinary tract, not now available by the current diagnostic procedures in general use.

The terms nephrogram and renogram have been used interchangeably to denote opacification of the renal shadows due to the presence of a urographic medium in either the finer elements of the renal vasculature or the various segments of the nephron, or both. The phenomenon was observed early in the development of the excretory urogram[1, 2, 3] as an inconstant faint shadow, usually associated with obstructive uropathy. Several investigators[4, 5, 6] noted the appearance of a parenchymal outline quite frequently in delayed films of patients with ureteral colic. This presumably was due to sudden increased intrapelvic pressure and a subsequent depression of glomerular filtration but continued transport of the medium across the epithelium of the tubules into its lumen where it cannot be excreted, with resultant increase in concentration, which produces renal opacification. One group of investigators[7] found nephrograms produced in 43 per cent of patients with ureteral colic. Attempts to produce this effect as a clinical diagnostic test by artificial blocking of the ureter[8, 9, 10] met with some success, but the apparent disadvantages of instrumentation, difficulty in producing temporary ureteral obstruction safely, time consumption, and poor results have made dubious its practical value.

Production of nephrograms by the presence of contrast medium in the vascular bed of the kidney alone requires high blood concentration in the renal artery and is demonstrated best by translumbar aortography.[11, 12, 13, 14, 15, 16] This procedure has been found to be quite valuable as a diagnostic examination and is

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[1] Von Lichtenberg, A.: J. Urol., 25: 249, 1931.
[2] Wesson, M. B.: Am. J. Roentgenol. 28: 27, 1932.
[3] Jaches, L.: J.A.M.A., 95: 1409, 1930.
[4] Wilcox, L. F.: Am. J. Roentgenol., 34: 596, 1935.
[5] Braasch, W. F. and Doss, A. K.: J. Urol., 43: 617, 1940.
[6] Heilbrun, H. and Chittenden, G.: Radiology, 47: 51, 1946.
[7] Florence, T. J., Howland, W. S. and Weens, H. S.: J. Urol., 56: 284, 1946.
[8] Hickel, R.: J. d'urol., 52: 275, 1944.
[9] Weens, H. S. and Florence, T. J.: Am. J. Roentgenol., 57: 338, 1947.
[10] Leighton, R.: Radiology, 53: 540, 1949.
[11] Dos Santos, R., Lomas, A. C. and Caldas, J.: Med. Contemp. (Lisbon) 47: 93, 1929.
[12] Doss, A. K.: Texas State Med. J., 38: 227, 1942; J. Urol., 55: 594, 1946.
[13] Nelson, O. A.: Surg., Gynec. & Obst., 74: 655, 1942; J. Urol., 53: 521, 1945.
[14] Wagner, F. B.: J.A.M.A., 125: 958, 1944.
[15] Melick, W. F. and Vitt, A. E.: J. Urol., 60: 321, 1948.
[16] Smith, P. G., Rush, L. W. and Evans, A. T.: J. Urol., 65: 911, 1951.

considered by a number of urologists as probably the single most informative procedure in radiologic examination of the kidneys. The development of less toxic organic iodine compounds to replace sodium iodide[12, 15, 16] has unquestionably reduced the hazard of the examination but it remains a 'procedure of some magnitude'[17] and not suited to routine use in most situations. Its handicaps of requiring an anesthetic, special equipment, a team or 4 or more people, being expensive and the judicious respect of aortic puncture has, and will continue to prohibit its widespread acceptance. In our own experience the procedure has been found to be quite helpful and completely innocuous but the aforementioned disadvantages limit its indications and use.

The radiographic vascular demonstration of renal parenchyma by intravenous administration of organic iodine compounds was first noted by Steinberg[18] as an incidental finding during angiocardiography. Since then, this observation has been confirmed and utilized by Weens, et al.,[19] in a series of 35 cases to produce satisfactory nephrograms in 83 per cent of the cases. Fifty cubic centimeters of 70 per cent diodrast were employed, injecting in 2 seconds through a 12 needle with a Robb-Steinberg angiocardiographic syringe and taking serial films with a rapid cassette changer, starting at 6 seconds. No serious reactions were reported in this series and the study was limited largely to individuals without kidney disease, no clinical application being reported.

The technique used in our series was modified in two ways; first, elimination of some of the objections shared with translumbar aortography, i.e., special equipment, extra personnel, and expense, and secondly, a different medium (urokon sodium 70 per cent) was used to reduce toxicity and provide a higher iodine concentration, with resulting greater contrast. It was believed that if the procedure is to be of clinical value that it must be simple, inexpensive, quickly and easily done with routine equipment by no more than 2 people, to be of no greater hazard than other commonly employed diagnostic procedures, and to produce consistently good results.

TECHNIQUE

Variations in type and amount of medium, time of injection and intervals of exposure were used in standardizing the procedure. The following technique was found to be most practical without sacrificing quality of the examination and was used in most of the group:

1) Preparation as for excretory urography and take flat film on standard cysto- or x-ray table to assure correct technique.

2) Routine sensitivity test for organic iodine contrast media.

3) Pull patient down on table so that kidneys will be directly under center of tube.

4) Explain to patient that he will possibly feel transitory flush on injection of medium and to refrain from any motion and breathing when so instructed.

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5) Skin wheal with 1 per cent procaine over anticubital vein and insert 15 gauge needle on ordinary 50 cc Luer Lok syringe.

6) Inject 50 cc 70 per cent urokon sodium as rapidly as possible, which takes approximately 5 seconds. (Have barrel of syringe plunger moist, so as to insure smooth injection.)

7) Have patient stop breathing and take one film at 10 seconds from end of injection and second one as soon as cassette can be changed, which is approximately at 25 seconds. Exposure time should be as short as equipment permits

8) Re-position patient as for a plain x-ray and complete excretory urogram series, with films at 5, 10 and 15 minutes or variations as desired.

It may rarely be difficult to insert a 15 gauge needle in small veins, but this can usually be overcome. By testing with saline prior to injection, extravasation may be prevented, as extravasated medium in this concentrated form is very painful. The presence of blood containing the medium in other viscera may make film somewhat lighter than flat plate, and it is usually wise to raise the k.v. approximately 4 for the two nephrogram exposures.

The ordinary 50 cc Luer Lok syringe was used in most of the examinations in this series and provide satisfactory films, but injection is made easier and more rapid using a 50 cc Robb syringe, which is identical except for a larger outflow connector. If the ordinary syringe is used, the caliber of the outflow connector should be checked to insure its adequacy, as variations in size have been noted in different syringes.

MEDIA

The availability of a satisfactory medium is essential in this type examination. Its requirements differ somewhat from those of aortography, as the intravenous injection, with its unavoidable dilution by blood, prohibits the extremely high renal artery concentrations obtained by translumbar puncture. This factor makes necessary the highest iodine content obtainable in the injected medium to provide an adequate degree of contrast. Another difference is that media used for nephrography must produce a minimum amount of side reactions in the unanesthetized patient, i.e., nausea, vomiting, arm pain, taste, flush, urticaria, etc., which may be annoying and associated motion during film exposure results in blurring, whereas in translumbar aortography these effects are of little consequence as the patient is asleep. Accordingly the ideal medium for nephrography would be: 1) Nontoxic, both as to producing anaphylaxis or other severe reactions and as to production of side reactions such as nausea etc.; 2) high iodine content; 3) freely soluble, so as to permit rapid injection; 4) stable in solution; and 5) inexpensive.

Urokon sodium 70 per cent* appears to most nearly approch this ideal by virtue of its high iodine concentration (table 1) and the clinical finding of its low toxicity when used for routine excretory urography.[20]

Both 75 per cent neo-iopax and 70 per cent diodrast were used in a few cases.

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Vascular nephrograms were produced with each, but the contrast appeared to be less than with urokon and in one patient in which diodrast and urokon both were used 3 days apart with the same technique, urokon unquestionably produced better films.

The dosage of 70 per cent urokon administered is approximately 500 mg./kg. and although this is approximately five times the quantity used in routine excretory urography, it is approximately one-eighteenth of the MLD.[21] (It has been found[22] to cause less tissue reaction when injected intramuscularly than 30 per cent urokon, diodrast or neo-iopax.)

RESULTS

This method of examination has been used in 80 cases to date without failure to opacify the renal parenchyma. A practical technique for clinical use as described above was evolved in this series and a wide variation in quality of the films was observed. Technical difficulties were encountered, particularly determination of proper time of injection and interval of exposure. Motion associated with breathing and rarely coughing caused blurring of one of the films in some instances, but at least one satisfactory film was obtained in each patient, and with the present technique, consistently good films are produced.

TABLE 1. *Relative iodine content in available concentrated urographic media*

	GM. MEDIA/CC	GM. IODINE/CC	GM. IODINE/50 CC
Urokon sodium 70%	.70	4606	23 03
Neo-iopax 75%	.75	.3862	19.31
Diodrast 70%	.70	3486	17.33

In approximately 50 per cent of the cases the great vessels and renal arteries are demonstrated in the first film. The circulation time of normal individuals varies, which makes consistent exposure of film at optimum time difficult with standard urological x-ray equipment (but could be done with the rapidograph or other serial rapid exposure devices). However, the degree of opacification produced by the medium in the finer vessels of the kidney appears to parallel the renal artery blood flow and produces an equivalent amount of information. The 20–25 second film usually gives maximum renal opacification.

The excretory urograms obtained in this method were found to be of excellent quality (figs. 1 and 2) and adequate for diagnosis in a much higher percentage of cases than previously reported by excretory urography. Filling of the pelves and ureters with a clear outline of the entire collecting system was frequently noted. Opportunity to compare pictures obtained in this examination with routine excretory urograms previously made was present in 16 cases and without exception showed improvement in the demonstration of the upper urinary tract (fig. 2). This finding suggests that present techniques for excretory urography do not make available the maximum concentration of organic iodine contrast

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[21] Nesbit, R. M. and Lapides, J.: Univ Mich Med. Bull , 16: 37, 1950.
[22] Byrne, J. E. and Melick, W. F. Urol. & Cutan. Rev., 55: 193, 1951.

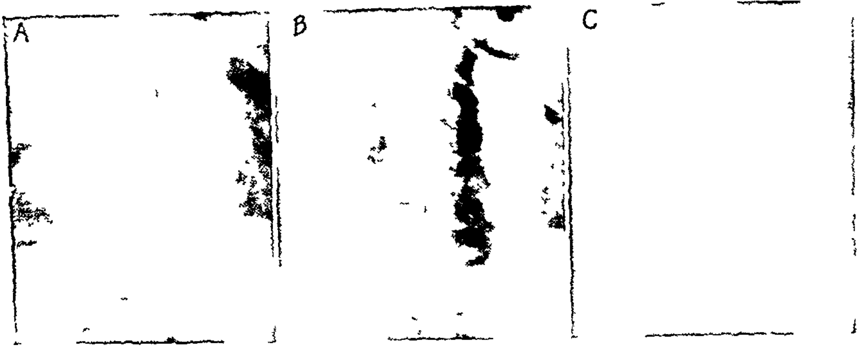

FIG. 1. Normal nephrogram Woman aged 50. *A*, flat film. *B*, nephrogram 25 seconds after injection. *C*, pyelogram 10 minutes after injection

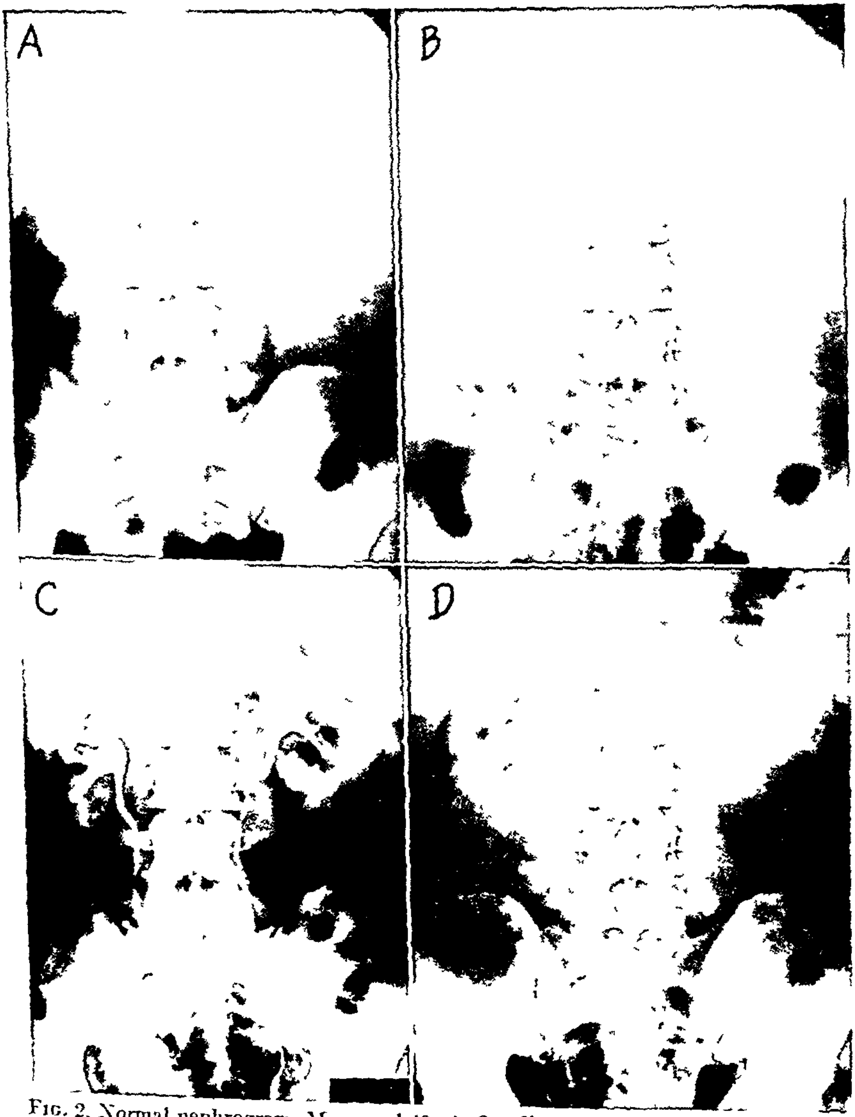

FIG. 2. Normal nephrogram Man aged 46. *A*, flat film. *B*, nephrogram 25 seconds after injection. *C*, pyelogram 10 minutes after injection. *D*, routine excretory urogram made 5 days previously with same preparation.

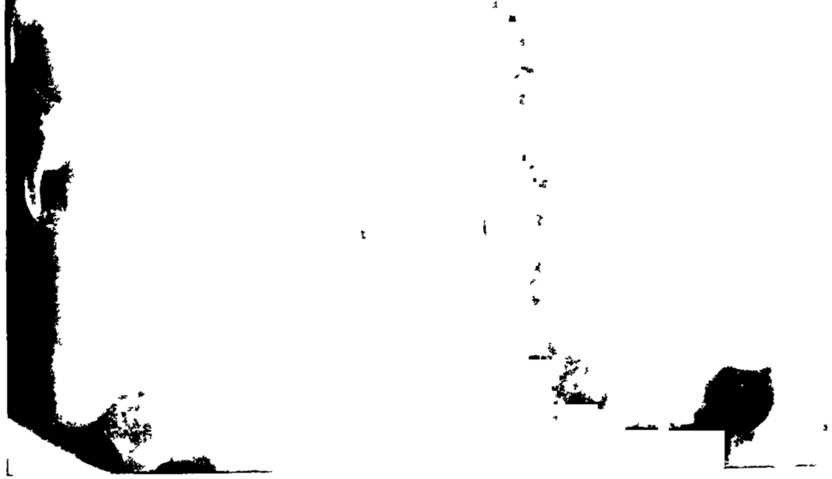

Fig. 3. Normal cholecystogram. *A*, 2 hour film showing contrast medium still present in renal pelvis overlying gallbladder. *B*, 4 hour film, same patient.

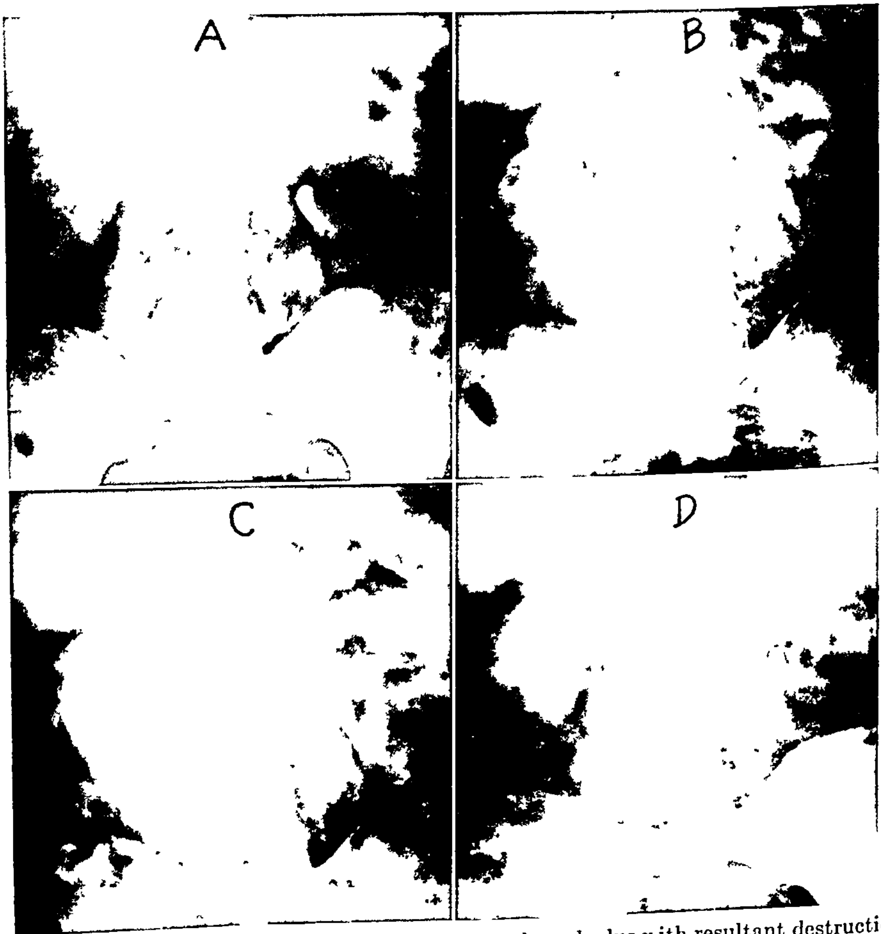

Fig. 4. Obstruction of left ureteropelvic juncture by calculus with resultant destruction of kidney. Woman aged 58. *A*, flat film *B*, nephrogram 10 seconds after injection showing aorta and renal artery on right, none on left *C*, nephrogram at 25 seconds showing no kidney shadow on left. *D*, pyelogram 10 minutes after injection. Nonfunctioning hydronephrotic sac found at exploration.

media that the normal kidney can utilize to produce shadows of the collecting system.

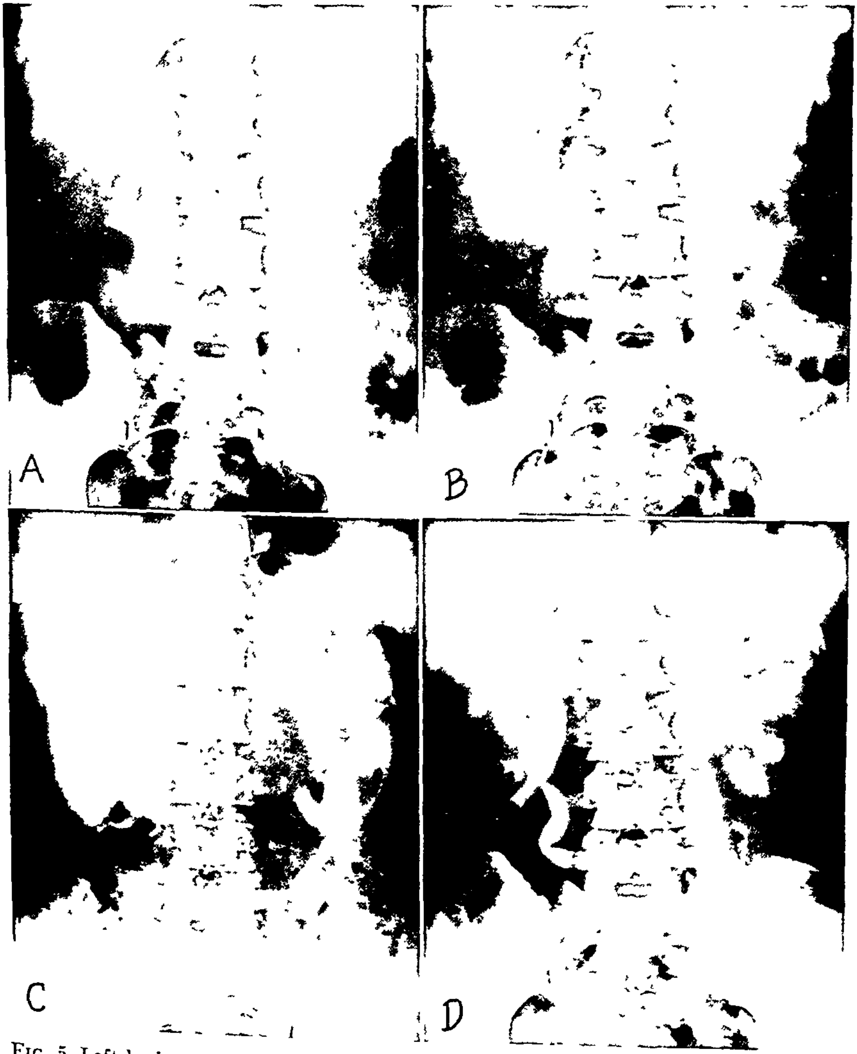

FIG. 5. Left hydronephrosis secondary to stone in lower third of ureter. *A*, flat film. *B*, nephrogram at 25 seconds after injection showing good blood supply on right, with less density on left, but fair nephrogram present. *C*, nephrogram produced by translumbar aortogram showing slightly greater bilateral density, but same relative degree. *D*, excretory urogram 15 minutes after nephrogram. (Calculus removed by cystoscopic manipulation and kidney left in place, since blood supply indicated satisfactory potential function.)

Abdominal arteriography by intravenous injection opacifies other viscera of the abdomen, but none as consistently or as well as the kidneys. The spleen and liver usually cast discrete shadows and aneurisms or anomalies of the abdominal aorta may be seen. An interesting incidental finding was the appearance of a good quality gallbladder shadow at approximately 1 hour with good visualization usually at 2, 3, and 4 hours (fig. 3).

In this series 42 per cent of the cases had intrinsic renal disease and 58 per cent proved to have normal upper urinary tracts. Cases were not selected for indications while technique was being developed. An attempt to evaluate the procedure by correlation with aortography, renal function tests, retrograde pyelography and pathological specimens in certain patients with kidney disease is being made and will be reported later. To date nephrography has been used largely in evaluation of the surgical kidney, i.e., calculous disease (fig. 4), hydronephrosis (fig. 5), renal tumors, pyelonephritis, tuberculosis and congenital anomalies. It also has been used to differentiate renal and extrarenal masses and to evaluate nonfunctioning kidneys in which ureteral catheterizations cannot be accomplished.

REACTIONS

No adverse reactions of consequence have occurred in this series. The usual side effects associated with excretory urography have been observed with certain exceptions and differences. Almost all patients experienced a transient feeling of warmth and flush and noted a foreign metallic-like taste. The incidence of nausea was surprisingly low with only 9 patients or 11.2 per cent and only 2 patients vomited, one a pregnant woman (5½ months), who appeared to be unusually susceptible. One patient had back pain for approximately 30 seconds following the injection. Five patients complained of transient headache and a mild urticaria was observed in 2 patients. No instances of arm pain due to venospasm were observed, but pain at the site of injection occurred in 7 patients in which some of the medium was extravasated into the tissues. This caused excruciating pain and the procedure should not be attempted unless a clean venopuncture is obtained. Iodism or syncope were not observed; however, no patients with history of allergy, severe systemic disease or marked renal impairment were used. Blood pressure changes were observed in a few patients and response varies from a drop of 10 mm. to a rise of 20 mm. mercury. The low incidence of nausea and vomiting in this procedure employing rapid injection of relatively large amounts of urokon sodium would seem to indicate that there is no relation between injection time of the medium and the incidence of this type of reaction, except to suggest that the occurrence probably is lower with rapid injection.

CONTRAINDICATIONS

The only absolute contraindications to the procedure probably are marked renal insufficiency, known allergy (including previous severe reaction to organic iodine compounds) and inadequate veins to permit venopuncture with a No. 15 gauge needle.

In this series ages varied from 10 years to 73 years. Patients with various associated diseases were used, including diabetes, hypertension, cardiac failure, tuberculosis, and pregnancy. No patient with severe systemic diseases, marked anemia, history of previous reaction to organic iodides, asthma, or uremia were used. (It is suggested that patients with liver disease and hyperthyroidism should be approached with caution.)

VALUE AND INDICATIONS

Intravenous nephrography is being investigated and presented as an examination that is almost as informative as translumbar aortography and without the disadvantages that have restricted its acceptance as a routine diagnostic procedure; namely, anesthesia, time and personnel requirements, special equipment, expense and supposed hazard of translumbar puncture.

This method is not proposed as a substitute for translumbar or femoral catheterization arteriography in certain cases as the concentration of medium and the resultant contrast provided is not as great in the intravenous method. The consistent demonstration of the renal arteries and their branches and as dense a renogram is not provided and cannot be expected to be as valuable in differentiation of intrarenal lesions or in diseases in which sharp delineation of the large vessels is essential. such as differentiating renal tumor and cysts or evaluation of ananomalous vessels. In certain other applications, the procedure appears to provide an equivalent amount of information.

The clear cut indications for vascular visualization of the kidney possibly are limited to differentiation of renal and extrarenal lesions, evaluating certain anomalies for surgery (horseshoe kidney, ectopia, etc.) and evaluation of nonfunctioning kidneys that cannot be catheterized. However, the procedure's single most valuable contribution probably will be as a test of differential renal function, particularly in preoperative study of kidneys in which conservative renal surgery is contemplated or considered. At least some investigators[12] believe that more information as to the functional integrity of a kidney can be obtained by preoperative radiologic demonstration of blood supply than can be obtained at surgical exploration.

Miscellaneous other uses of the procedure closely parallel those of translumbar arteriography and its value in many urologic diseases will be demonstrated only with further application.

SUMMARY

The availability of a nontoxic medium with higher iodine concentration has made possible a practical clinical method of radiologic demonstration of the renal parenchyma. Rapid intravenous injection of 70 per cent urokon sodium has been found to consistently produce satisfactory opacification of the kidney with minimal toxic side effects. A simplified technique is described that can be incorporated into routine excretory urography, eliminating most of the disadvantages of translumbar aortography, yet providing almost as much information regarding the status of the upper urinary tract. The procedure is not designed to supplant aortography in cases in which visualization of the renal vessels is essential, but does provide a similar amount of information as well as a test of differential renal function and differentiating renal and extrarenal lesions.

This procedure has been used in 80 cases with opacification of the renal outlines in each instance. No serious reactions were observed, the most troublesome being pain caused by accidental extravasation of the medium in 7 cases. A transient vasomotor flush and feeling of warmth were consistently present and the incidence of nausea and vomiting was comparable to that usually seen in good quality gallbladder shadow at approximately 1 hour with good visualization usually at 2, 3, and 4 hours (fig. 3).

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CONCLUSIONS

1) A technique of vascular visualization of the renal parenchyma is described employing rapid intravenous injection of 70 per cent urokon sodium, which can be incorporated into routine excretory urography by simple modifications.

2) The method has been used in 80 cases with no serious reactions and without failure to produce a nephrogram.

3) Clinical applications are discussed and comparisons made with other methods of renal arteriography.

4) Excellent excretory urograms are obtained by this method indicating that present routine dosages for excretory urography do not provide the maximum amount of organic contrast medium that can be utilized to outline the collecting system.

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INFLUENCE OF ALUMINA GELS ON PREVENTION OF URINARY CALCULI

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The origin of urinary calculi has been extensively studied but remains largely obscure. Obstruction, infection, hyperexcretion of crystalloids,[1] and subepithelial plaque formation[2] are frequently associated but no single etiologic agent is common to all cases; probably multiple factors are involved. Renal stone may occur with hyperparathyroidism, oxaluria, cystinuria, milkman syndrome[3] and other metabolic disorders, but in the majority of patients chemical studies fail to establish the presence of an underlying disturbance in metabolism. Except for the small group in whom stone formation results from metabolic abnormality (and for whom surgical removal of the cause, as of hyperfunctioning parathyroid tissue, is usually curative) renal stones are prone to recur after excision and to increase in size despite all known preventive measures. The treatment most commonly employed has attempted to reduce urinary phosphate precipitation by continuous acidification of the urine. For this purpose it has been customary to utilize acid-ash diets, usually supplemented by acidifying agents. However, this treatment is too often limited in effectiveness by the presence of ammonia-forming organisms in the urinary tract, and impairment of renal function. Under such circumstances a highly acidifying regimen is hazardous because of the danger of acidosis. In many patients with urinary infection no amount of acidification will reduce the urinary pH to the desired acid range. The urine will remain acid until it reaches the kidney pelvis, where it will become alkaline through bacterial production of ammonia from urea. Hence, the serious hazards of secondary operations of the kidney[4] for many patients have been inescapable.

The present study was undertaken 1) to confirm the value of certain alumina gels in preventing formation and enlargement of renal stone; and 2) to determine the metabolic role of magnesium in the development of urinary calculi.

ALUMINA GEL FOR CONTROL OF RENAL CALCULI

Rationale. In passing through the gastro-intestinal tract the aluminum combines with phosphate ions to form an insoluble aluminum phosphate which is entirely excreted as such in the stool, thus diminishing the amount of phosphate available for resorption through the alimentary tract. Decreased intestinal resorption of phosphate lowers the serum inorganic phosphorus, favors a more complete tubular resorption of phosphate ions, and hence reduces urinary ex-

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Submitted in partial fulfillment of the requirements for the degree of Doctor of Medical Science.

[1] Keyser, L.: Etiology of urinary lithiasis. Arch. Surg., 6: 525, 1923.

[2] Randall, A.: Papillary pathology as a precursor of primary renal calculus. J. Urol., 44: 580, 1940.

[3] Albright, F., et al.: Osteomalacia and late rickets. Medicine, 25: 399, 1946.

[4] Goldstein, A. E.: Secondary renal operations. Am. J. Surg., 80: 405, 1950.

cretion of phosphate.[5] In short, phosphate is eliminated largely in the stool rather than in the urine, the extent of the change depending on the dosage of alumina gel and restriction of phosphorus intake.

Freeman and Freeman, first to use aluminum hydroxide gel to reduce urinary phosphorus excretion, reported, in 1941,[6] a reduction in concentration of inorganic phosphorus in the serum and urine of a series of children with chronic renal insufficiency, and also in the control—a child with normal kidneys. By administering 120 cc daily in four equal doses, they succeeded in restoring the hyperphosphatemia and hypocalcemia to normal values in the children with uremia.

In 1945, Ephraim Shorr[5] described a patient with bilateral staghorn phosphatic calculi, whose urinary tract was grossly infected with a urea-splitting organism resistant to chemotherapy, and for whom an acidifying regimen would have been futile. Administration of 120 cc amphojel* daily reduced the urinary phosphorus excretion by 90 per cent. Shorr suggested that diversion of the phosphorus from the urine to the intestinal tract might inhibit enlargement of existing phosphatic calculi and prevent formation of new stones.

METABOLIC ROLE OF MAGNESIUM

The metabolic role of magnesium in the development of renal stone was first studied by Greta Hammersten.[7] In extensive experiments on rats she showed that an acidotic diet high in oxalic acid but deficient in magnesium and vitamins A and D would produce calcium oxalate calculi in the presence of acid urine; and calcium phosphate stones if the urine were alkaline. Conversely, after feeding the rats, in which stones had formed, a "therapeutic" diet lacking oxalic acid but ample in magnesium and vitamins, decalcification of the stones was demonstrated by x-ray in two thirds of the animals. In further studies she found that magnesium, by forming a complex, readily soluble compound with the oxalate ion, greatly increased the solubility of calcium oxalate. Survey of the literature failed to reveal any confirmation of these animal experiments, and no clinical application. They suggest, however, that in the human, deficiency of magnesium may lead to increase in excretion, and an adequate supply of magnesium to lessened excretion, of endogenous oxalic acid.[8]

CLINICAL PROCEDURE

From the urological outpatient clinic, 34 patients were selected who 1) were suffering from recurrent urinary calculi and who had no apparent metabolic disorder (some had had three to five operations for removal of renal or ureteral stones); 2) had gross infection of the urine, resistant to chemotherapy; 3) had calculi containing phosphate salts as the major component; or 4) had undergone operation for recurrent calculi and in whom prevention of further stone formation was desired.

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* Amphojel ®, aluminum hydroxide gel (alumina gel), supplied by Wyeth Incorporated.

[5] Shorr, E.: Possible usefulness of estrogens and aluminum hydroxide gels in the management of renal stone. J. Urol., **53**: 507, 1945.

[6] Freeman, S. and Freeman, W. M. C.: Phosphorus retention in children with chronic renal insufficiency; effect of diet and ingestion of aluminum hydroxide. Am. J. Dis. Child., **61**: 981, 1941.

[7] Hammersten, G.: Dietetic therapy in formation of calcium oxalate calculi in urinary passages. Skandinav. Arch. f. Physiol., **80**: 165, 1938.

[8] Hammersten, G.: Bildningen av. aseptiska urinvagastener sartryck. Nord. Med., **30**: 911, 1946.

Treatment was as follows: 1) Fluid intake was raised (8 to 10 glasses of water daily). 2) A constant maintenance diet (see tables 1 and 2) was instituted, which contained 0.6 gm. calcium, 1.2 gm. phosphorus, and 0.246 gm. magnesium per day. This diet supplied about 1800 calories, with neutral or slightly acid ash. 3) Vitamin A concentrate was administered, in daily doses of 50,000 units for the first month, and 25,000 units thereafter. 4) Amphojel with magnesium trisilicate,* in doses of 30 to 45 cc was given 4 times daily in half a glass of water. 5) At monthly intervals the 24 hour urinary output was analyzed for inorganic phosphorus, by a modification of the Fiske and SubbaRow method[3] (see p. 319); and to check on the completeness of the urine collection, the 24 hour urinary creatinine excretion was determined. (Normally, females excrete from 14 to 22 mg., and males from 20 to 28 mg. of creatinine per kilogram of body weight

TABLE 1. *Maintenance diet of calcium and phosphorus*

Use daily in the amounts stated:
- 1½ glasses milk, ½ glass at each meal
- 4 ounces meat or fish
- 2 eggs
- 6 slices white bread
- 2 portions cereal, see list
- 3 servings fruit, see list; one must be orange or grapefruit
- 2 vegetables, see list

Foods permitted:

Meat and Fish: Beef, chicken, ham, lamb, pork, veal, codfish, flounder, haddock, halibut.

Vegetables: Artichokes, French; asparagus; beans, string or snap; beets, cabbage, carrots, cauliflower, celery, cucumbers, eggplant, endive, escarole, lettuce, okra, onions, parsnips; peppers, green; potatoes, white and sweet; radishes; squash, summer and winter; tomato, turnips.

Fruit: Apples, apricots, avocado, banana, blackberries, blueberries, cantaloupe, cherries, cranberries, currants, dates, gooseberries, grapefruit, grapes, huckleberries, lemons, loganberries, muskmelon, oranges, peaches, pears, persimmons, pineapple, plums, prunes pumpkin, raisins, raspberries, rhubarb, strawberries, watermelon.

Cereals: Farina, cream of wheat, cornflakes, rice krispies, cornmeal, oatmeal, white rice, macaroni, spaghetti.

Foods permitted in unlimited quantities: Sugar, jelly, butter, vinegar.

Do not use: Cereal, fruit, or vegetables except those listed above; nuts of any kind, including peanut butter; cheese, except cottage or pot; heart, liver, bluefish, clams, mackerel, salmon, shrimp, turkey, kidney, smelt, sardines, fish roe; cocoanut; figs; maple syrup, molasses, Karo; gelatin, yeast.

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* Amphojel ®, aluminum hydroxide (alumina gel), with magnesium trisilicate, containing 4 per cent aluminum oxide and 12.5 per cent magnesium trisilicate, was made available by Wyeth Incorporated.

cretion of phosphate.[5] In short, phosphate is eliminated largely in the stool rather than in the urine, the extent of the change depending on the dosage of alumina gel and restriction of phosphorus intake.

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[8] Hammersten, G.: Bildningen av. aseptiska urinvagastener sartryck. Nord. Med., 30: 911, 1946.

The plan was as follows: 1) During the 6 day *fore period*, in the *first* 3 days (adjustment period) the patients received the maintenance diet only; in the *second* 3 days the maintenance diet was fed and 24 hour specimens of food, urine, and stool were collected. 2) Then followed two *experimental periods* of 3 days each. In the *first* (period 1) the patients received the maintenance diet and plain amphojel, 30 cc, 4 times daily; 24 hour specimens of food, urine and stool were collected. In the *second* (period 2) the patients received the maintenance diet and amphojel with magnesium trisilicate, 30 cc 4 times daily; 24 hour specimens of food, urine and stool were collected. 3) In the 2 day final or *recovery period* (period 3) for observation of the return to normal values, the patients received only the maintenance diet; 24 hour specimens of food, urine and stool were collected. To maintain positive nitrogen balance, all were allowed to be up and about the ward 4 to 6 hours a day.

Blood was withdrawn on the last day of each period for calcium, phosphorus and magnesium determinations. The urine was collected in 24 hour volumes and the pH determined with nitrazene paper. It was then acidified with 5 cc glacial acetic acid, measured, and a portion pooled for each period.

METHODS OF ANALYSIS

Inorganic phosphorus in the urine was determined by the following modification of Fiske and SubbaRow method.

A 1:5 dilution of the urine gave the best colorimetric range. One cubic centimeter of this dilution was placed in a 50 cc flask and half the amount of the other reagents used (see Fiske and SubbaRow method[9]). The determinations were done in duplicate. A phosphate standard (KH_2PO_4 1.0 cc, containing 0.08 gm. phosphorus) was carried along with each set of unknowns, and these were read against a reagent blank on an Evelyn photoelectric colorimeter with a 540 filter. The galvanometer scale measuring the percentage of transmission was in 24 hours.) 6) Roentgen examination of the urinary tract was performed every 3 months.

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[9] Fiske, C. H. and SubbaRow, Y.: Determination of phosphorus. J. Biol. Chem., 66: 375, 1925.

Method of Fiske and SubbaRow for the determination of inorganic phosphorus in urine. Measure into a 100 cc volumetric flask enough urine to contain between 0.2 and 0.8 mg. inorganic phosphorus (usually 1 or 2 cc). (Accurate results can be obtained, with proper care, using as much as 1.6 mg. phosphorus.) Add water to bring the total volume to 70 cc, followed by 10 cc of Molybdate 1 and 4 cc of 0.25 per cent aminonaphtholsulfonic acid. (Molybdate 1: 2.5 per cent ammonium molybdate in 5 N sulfuric acid. Dissolve 25 gm. of the salt in 200 cc of water. Rinse into a liter volumetric flask containing 500 cc of 10 N sulfuric acid. Dilute to the mark with water and mix.) After the addition of each reagent, the solution should be mixed by gentle shaking.

At the same time transfer to a similar flask 5 cc. of the standard phosphate solution (containing 0.4 mg. phosphorus), 65 cc water, and the same reagents that were added to the urine sample. Dilute the contents of each flask to the mark, mix, and compare in the colorimeter after 5 minutes.

The Evelyn photoelectric colorimeter, which is more accurate than the visual colorimeter originally used by Fiske and SubbaRow, was used for the determinations in this study.

Balance studies to determine the role of magnesium in the formation of urinary calculi were conducted on 3 patients from this group. Two, a male (R.) and a female (M.), had renal calculi; and 1 female (S.) had permanent bilateral nephrostomies, because of ureteropelvic obstruction, after removal of stones from

TABLE 2. *Daily menu showing caloric value and the breakdown of carbohydrate, protein and fat*

	MEASURE (GRAM)	CARBOHYDRATE (4 CALORIES PER GRAM)	PROTEIN (4 CALORIES PER GRAM)	FAT (9 CALORIES PER GRAM)
Breakfast				
Fruit, 15% of meal	100	15	1	—
Eggs	2	1	13	12
Cereal	50	4	1	—
Bread, white	60	30	6	2
Butter	20	—	—	19
Milk	100	5	4	4
				55 25 37
Lunch				
Meat	60	—	16	11
Vegetables	100	6	2	—
Bread, white	60	30	6	2
Butter	20	—	—	19
Milk	100	5	4	4
Fruit, 15% of meal	100	15	1	—
				56 29 36
Dinner				
Meat	60	—	16	11
Vegetables	100	6	2	—
Bread, white	60	30	6	2
Butter	20	—	—	19
Milk	100	5	4	4
Fruit, 15% of meal	100	15	1	—
				56 29 36
			Total	167 83 109 ×4 ×4 ×9 668 + 332 + 981
				Total Calories—1,981

Tea may be used if brewed with distilled water.

both kidneys. In this patient the right kidney functioned only slightly, and a large amount of sand and numerous stones had passed through the left nephrostomy tube, but at the start of this study she was free from calculi. The control was a healthy female office worker (D.) with normal kidneys.

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$$\frac{\text{Unknown}}{\text{Standard}} \times \frac{0.08}{1\ \text{cc}} \times 24 \text{ hour volume} = \begin{array}{l}\text{milligrams of}\\ \text{phosphorus per}\\ \text{24 hours}\end{array}$$

The calculated error was found to be less than 2 per cent by the recovery methods.

Total phosphorus was determined on all samples of serum, food and stool. For the serum determinations, the Fiske and SubbaRow[9] method was used according to the original description, but modifications were adapted for the other specimens. A wet ash procedure was done, in triplicate, in NPN tubes, on all samples of food and stool, as follows:

Five cubic centimeters of food were diluted to 15 cc and 1 cc was ashed. Ten cubic centimeters of stool were diluted to 100 cc and 1 cc was ashed. Seven-tenths of a cubic centimeter of concentrated sulfuric acid was added to each NPN tube which was heated over a microburner. After clearing had developed by the dropwise addition of concentrated nitric acid, it was transferred to a 50 cc volumetric flask with distilled water. Except for the use of Molybdate 3 reagent (without acid) instead of Molybdate 1 (with acid), the procedure was the same as for inorganic phosphorus. The unknowns were read against a reagent blank which was also ashed. It was found that the ashed standard gave the same reading as a standard prepared for inorganic phosphorus using Molybdate 1; hence, the latter was used for the sake of convenience. The calculated error by the recovery method was found to be less than 5 per cent.

Creatinine. The Lynch modification of the Folin[10] method (omitting the precipitation of protein) was used on a twenty-four sample of urine.

Total magnesium. The molybdivanadate method for determination of magnesium in serum was published by Simonsen[11] at the time the previous laborious methods were proving unsatisfactory for these determinations. By using the wet ash preparation for the food, urine and stool specimens, application of the molybdivanadate method afforded a simplified procedure for completing magnesium determinations within twenty-four hours. This procedure was found to be sufficiently accurate by doing recoveries on various samples (tables 3, 4, 5 and 6).

Total calcium was determined in triplicate by microtitration with potassium permanganate, after the method of Tisdall and Kramer.[12] In the second experimental period (period 2) and in the recovery period (period 3), when amphojel with magnesium trisilicate was present, it was impossible to make chemical

[10] Folin, O.: Determination of creatinine and creatine in urine. J. Biol. Chem., **17:** 469, 1914.

[11] Simonsen D. G., et al.: Determination of serum magnesium by the molybdivanadate method for, phosphate. J. Biol. Chem., **169:** 39, 1947.

[12] Tisdall, F. F. and Kramer, B.: Direct quantitative determination of sodium, potassium and magnesium in urine and stool. J. Bil. Chem., **48:** 1, 1921, quoted by Peters and Van Slyke, Quantitative Clinical Chemistry, vol. II, p. 764, Williams & Wilkins, 1932.[17]

determinations of the stool calcium because at that time there was no known method for determining calcium in the presence of large quantities of magnesium. Fales' method[13] of differential precipitation was tried without success. The flame photometer, using lithium as an internal standard, was also unsuccessful because phosphate compounds gave unpredictably low readings for the calcium. Spectrographic analysis was considered but there was insufficient time for preliminary determination of accuracy. In the first experimental period (period 1), when plain amphojel was given, fecal calcium was determined on only one balance study, and the accuracy of this finding was questionable.

TABLE 3. *Recovery of magnesium added to serum*

MG. ADDED (GAMMA)	MG. FOUND (GAMMA)	MG. CALCULATED (GAMMA)	RECOVERY %
0.0	43.0		
40.0	81.0	83.0	97.5
60.0	105.0	103.0	102.0
80.0	126.0	123.0	102.0
90.0	133.0	133.0	100.0

TABLE 4. *Recovery of magnesium added to urine*

MG. ADDED (GAMMA)	MG. FOUND (GAMMA)	MG. CALCULATED (GAMAM)	RECOVERY %
0.0 1st sample	81.0		
30.0	112.0	111.0	100.9
0.0 2nd sample	122.0		
50.0	172.0	167.0	102.9

TABLE 5. *Recovery of magnesium added to stool*

MG. ADDED (GAMMA)	MG. FOUND (GAMMA)	MG. CALCULATED (GAMMA)	RECOVERY %
0.0 1st sample	46.0		
30.0	82.0	76.0	107.3
0.0 2nd sample	36.0		
50.0	86.0	86.0	100.0
0.0 3rd sample with aluminum hydroxide present	54.0		
50.0	102.0	104.0	98.0

TABLE 6. *Recovery of magnesium added to food*

MG. ADDED (GAMMA)	MG. FOUND (GAMMA)	MG. CALCULATED (GAMMA)	RECOVERY %
0.0	41.0		
50.0	93.0	91.0	102.0

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[13] Fales, H. A.: Inorganic Quantitative Analysis, New York, Century Co., 1925.

The calculated error on calcium determinations by actual recoveries was found to be less than 5 per cent for food, 6 per cent for urine, 6 per cent for stool and 1 per cent for serum.

TABLE 7. *Result of balance studies on 3 calculous patients and 1 control*

		Calcium					Phosphorus					Magnesium					Creatinine mg./24 hrs
		Serum mg. %	Intake mg./day	Output, mg./24 hr.		Balance	Serum mg. %	Intake mg./day	Output, mg./24 hr.		Balance	Serum mg. %	Intake mg./day	Output, mg /24 hr.		Balance	
				Urine	Feces				Urine	Feces				Urine	Feces		
Fore period, 3 days Maintenance diet	D	10.1					3.4					1.9					
	R	9.6					3.7					2.1					
	M	10.6					4.0					2.0					
	S	10.3					4.2					2.1					
Fore period, 3 days Maintenance diet	D	10.4	671	187	849	−365	3.9	1233	776	491	−34	2.1	164	119	190	−145	978
	R	9.7	742	91	643	+8	3.7	1268	736	445	+87	2.0	138	56	154	−72	807
	M	11.1	351	67	438	−154	4.6	1080	626	459	−5	2.0	189	63	115	+11	975
	S	10.4	628	43	397	+189	3.8	945	711	179	+10	1.9	148	23	89	+37	743
Period I, 3 days Maintenance diet + 120 cc plain amphojel	D	10.3	689	171	—	—	3.7	1236	280	365	+591	1.9	163	73	81	+9	1050
	R	9.5	648	68	—	—	2.6	1178	424	299	+455	1.9	142	31	76	+35	717
	M	10.2	439	63	—	—	3.8	1300	258	833	+209	2.0	151	75	82	−6	897
	S	10.4	623	57	—	—	3.4	1026	360	315	+351	1.9	140	29	72	+39	732
Period II, 3 days Maintenance diet + 120 cc amphojel & mag. trisilicate	D	10.1	623	173	—	—	3.7	1160	263	596	+301	2.2	125 1824 1949	123	754	+1072	880
	R	9.7	652	164	—	—	3.6	980	148	1219	−387	2.1	148 1824 1972	110	864	+998	774
	M	10.5	418	102	—	—	3.5	1155	124	680	+351	2.5	153 1824 1977	262	457	+1258	900
	S	10.3	654	74	—	—	3.7	1020	167	958	−105	2.1	132 1824 1956	56	1202	+698	793
Period III, 2 days Recovery Maintenance diet	D	10.4	646	199	—	—	4.4	1148	684	813	−349	2.2	181	171	1746	−1736	973
	R	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
	M	10.4	—	—	—	—	4.6	—	—	—	—	2.0	—	—	—	—	—
	S	10.6	643	79	—	—	4.1	1020	506	688	−174	1.8	137	45	1155	−1063	577

D—Control.
R—Recurrent rt. renal calculus.
M—Bilateral staghorn calculi.
S—Recurring lt. renal calculi

RESULTS OF THE BALANCE STUDY

Experimental observations are shown in table 7. Serum values for calcium and magnesium were practically unchanged throughout. Serum phosphorus remained essentially the same except for a slight rise in the recovery period (period 3).

Calcium. The daily intake of patients D., R., and S. averaged 657, 682 and 637 mg. respectively throughout the entire balance study. The diet was calculated to supply 663 mg. calcium per 24 hours. M.'s calcium intake averaged 402 mg. per day because of her difficulty in taking the diet as planned, but she ate all of each serving as the others were required to do. The urinary output of calcium for the 3 patients in the balance study was definitely lower than for the control. It remained low in period 1 (with plain amphojel) but increased in period 2 (when amphojel with magnesium trisilicate was given). These values parallel those for urinary magnesium, shown in figure 1, a graph of the average findings in the study. Fecal calcium could not be analyzed.

Phosphorus intake varied somewhat from one period to the next, but was relatively constant throughout, averaging from 1003 mg. (S.) to 1194 mg. (D., the control) per day. The diet was calculated to contain 1173 mg. per 24 hours. A rapid and definite reduction in urinary phosphorus output, recorded as inorganic phosphorus (which averaged 712 mg. in the fore period), occurred in all cases during periods 1 and 2, varying in amount from 66 to 81 per cent. In period 3 (recovery period), there was prompt return toward normal in 2 days (fig. 1). The decided increase in fecal phosphorus coincided with the decrease in urinary phosphorus output. In the recovery period these values returned toward normal.

Magnesium intake remained the most constant, the daily average ranging from 139 mg. (S.) to 164 (M.). The diet had been calculated to contain 246 mg. per day, or approximately 100 mg. more than the amount actually consumed. The value for magnesium ingested as magnesium trisilicate in period 2, amounting to 1824 mg. per day, was added to that for the dietary intake. The urinary magnesium output was low in the fore period for the experimental subjects (averaging 47 mg. per 24 hours, compared to 119 mg. for the control, D.), and remained fairly constant in period 1, but the control dropped to 73 mg. per 24 hours. In period 2 all showed a definite rise after ingestion of amphojel with magnesium trisilicate; in the control magnesium continued to rise during period 3 but in experimental subject S. decreased slightly. The fecal magnesium output dropped perceptibly in all cases during period 1 but increased greatly in period 2, the rise persisting in period 3 for the control but falling slightly for S.

In general, the balances were equally divided between positive and negative values during the fore period, the control (D.) being negative for all three minerals, and S. remaining positive throughout the experimental period. Phosphorus and magnesium balances were positive during amphojel therapy in all cases but in the recovery period were negative, as expected. Calcium balances could not be determined, except in the fore period, because of the absence of stool calcium values.

Creatinine.[17a] Neither the 3 experimental subjects nor the control were of muscular physique, and all were accustomed to sedentary occupations. The average daily urinary creatinine excretion of less than 1 gm., which remained relatively constant for all, was considered to indicate that complete 24 hour urine specimens had been collected.

RESULTS OF TREATMENT WITH ALUMINA GELS

In 2½ years' observation of the 34 patients receiving amphojel with magnesium trisilicate, treatment was successful in 30 (88.2 per cent); there was no evidence of new stone formation or enlargement of existing calculi, nor of decalcification of the skeleton or other ill effects. In 3 of the 30, stones that were present at the start of treatment passed or disappeared after use of amphojel with magnesium trisilicate for 4 to 12 months. In a fourth (C.R.) the stone became two-thirds smaller during treatment. Following are the details on patient C. R.

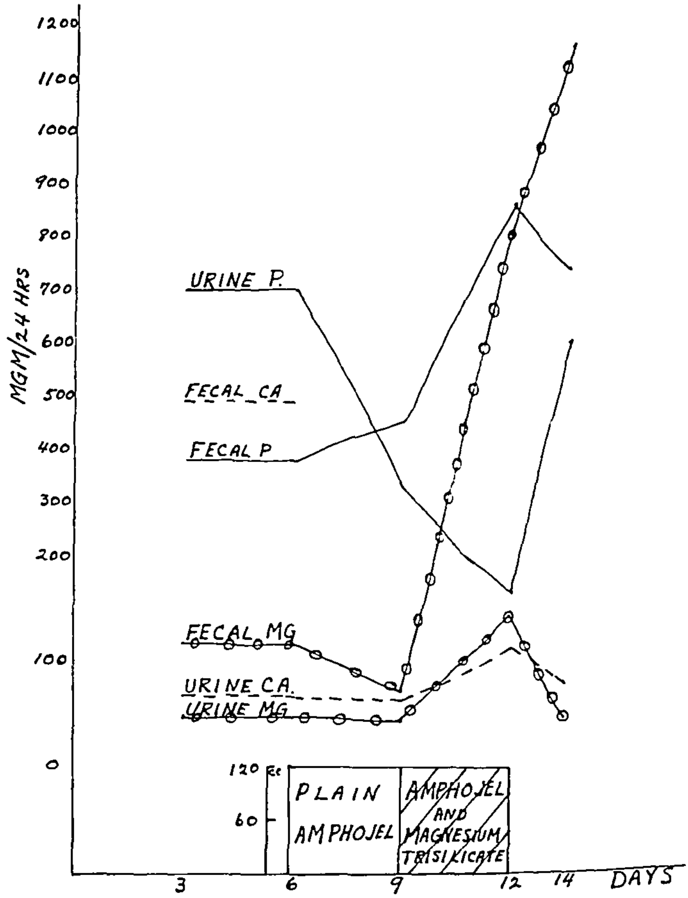

FIG. 1. Showing effect of amphojel on calcium, phosphorus and magnesium

C. R., a 69 year old white tailor, had a right ureterolithotomy in March 1945; a right pyelolithotomy in August 1945; and a cystolithotomy in 1946, all for calcium phosphate and carbonate stone. In the right kidney the calculus recurred (fig. 2, *A*) and by February 1947 had enlarged to greater than previous size (fig. 2, *B*). Results of chemical studies were within normal limits; urine culture revealed infection by urea-splitting organisms: Bacillus aerogenes and B. proteus. On April 2, 1947 he was started on a maintenance diet restricted in calcium and phosphorus, with vitamin A and 120 cc amphojel with magnesium trisilicate daily. He passed several small phosphate and carbonate stones on April 16, 1947. After 6 months on amphojel treatment, roentgen examination showed evidence of decalcification at the periphery of the stone (fig. 2, *C*); after 1 year, definite reduction in size. He continued to pass gravel and small calculi, and 17 months after start of treatment a flat film showed the stone was reduced to about two-thirds its original size (fig. 2, *D*). Urinary phosphorus excretion throughout 18 months of observation averaged 465 mg. per 24 hours.

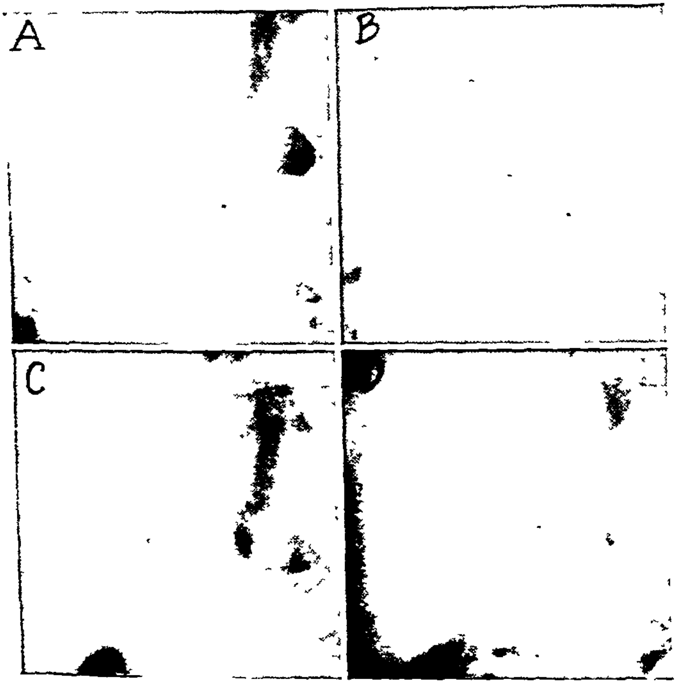

FIG. 2. Patient C. R. *A*, right renal calculus, March 1946, before treatment. *B*, right renal calculus, February 1947, increased in size before treatment. Amphojel with magnesium trisilicate started. *C*, right renal calculus after 6 months on amphojel. Note decalcification at periphery. *D*, right renal calculus after 17 months on amphojel. Note definite reduction in size.

Stone recurred in 1 (S.) and passed through a nephrostomy tube, and an existing calculus enlarged in 1 of the 4 patients who did not respond to treatment. However, these 2 took the alumina gel sporadically, as indicated by urinary phosphorus determinations. *This is the most likely cause for failure of the treatment.* In a third, who had a stricture of the ureter following ureterolithotomy, 2 stones formed above the obstruction. In the fourth patient, with idiopathic hypercalcinuria, the urinary calcium excretion had been twice the normal values before therapy. His stone recurred despite diet regulation and administration of alumina gel.

Nineteen of the patients in this series, before amphojel treatment, were excreting an average of 1.012 gm. inorganic phosphorus in the urine per 24 hours.

In these patients and in 5 others, after amphojel treatment, urinary phosphorus excretion had fallen to 0.451 gm. per 24 hours, a reduction of 56 per cent.

An interesting observation on 2 female patients in uremia suggests that to divert the phosphate through the gut, thus partially relieving the kidney of the necessity to eliminate phosphorus, may facilitate excretion of urea, with reduction of serum urea nitrogen.

A 72 year old woman (M.), one of the subjects used for the balance study, was admitted on December 27, 1946 suffering from bilateral staghorn calculi and with a serum urea nitrogen reading of 70 mg. per cent. She became progressively worse and semicomatose at times. On January 3, 1947 the urea having risen to 98 mg. per cent on supportive therapy alone, amphojel with magnesium trisilicate was started, in 4 daily doses totaling 120 cc. In 3 days the serum urea nitrogen dropped to 81 mg. per cent; in 7 days, to 39 mg.; in 14 days, to 26 mg.; and in 21 days it was normal at 14 mg. per cent. She also showed decided symptomatic improvement. Urea excretion remained normal on this therapy for more than a year, until she died from arteriosclerotic heart disease at another hospital. No change in the size of the calculi could be detected by x-ray during this period. The urinary phosphorus excretion averaged 118 mg. per 24 hours.

A 53 year old woman (P. R.) had a left nephrectomy for calculus pyonephrosis in 1942 at another hospital. Nine months after operation a large staghorn calculus had developed in the remaining right kidney. After an absence of 4 years this patient returned to the clinic (1946) with serum urea nitrogen reading of 23 mg. per cent, which by May 1947 had risen to 63 mg. per cent, with signs of early uremia. On her refusal to be hospitalized, she was placed on outpatient therapy with amphojel with magnesium trisilicate, and in 1 month the urea had dropped to 36 mg. per cent, remaining at about this level for the year she was subsequently under observations. Repeated x-ray examinations showed no change in the size of the stone. The urinary phosphorus excretion averaged 172 mg. per 24 hours.

Although it is preferable to maintain daily urinary phosphorus excretion at 200 mg. or less, satisfactory results have been achieved thus far in all patients treated by reducing the urinary phosphorus level to an average of 450 mg. per day. Several of the more cooperative patients have continued to adhere conscientiously to dietary restrictions so as to maintain excretion, on the minimum dosage of amphojel, at 200 mg. or less; but others, less careful of the diet, frequently require much larger amounts to hold the urinary phosphorus within the range of 450 to 200 mg. When, for this reason, the daily dose of amphojel must exceed 160 to 180 cc, patients may resist therapy because of the taste.

*Clinical use of basaljel.** To reduce the bulk of medication, minimize any possible tendency to constipation, and to insure the palatability necessary for agents used in large doses over prolonged periods a new formula, basaljel, has been developed at the suggestion of Ephraim Shorr. It contains a larger amount of aluminum and therefore has a greater phosphate-binding power in the bowel.

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* Basaljel ®, basic aluminum carbonate gel, was supplied by Wyeth Incorporated.

Shorr, Carter and associates[14] consider basaljel 33 per cent more effective than amphojel in reducing urinary excretion of phosphorus.

At this clinic 10 patients who had been receiving amphojel with magnesium trisilicate were placed on basaljel, 120 cc daily in 4 divided doses. Urinary phosphorus excretion has been reduced to lower levels than could have been obtained with amphojel in the same dosage. These initial results, to be confirmed, of course, by a longer period of observation, would indicate that basaljel is more effective than amphojel in prophylaxis of phosphatic stone. Shorr, Carter and associates,[14] having maintained, for more than 5 years, a group of about 20 patients on alumina gel and phosphorus-restricted diet, are greatly encouraged by the fact that existing calculi have not enlarged nor have new stones developed in those who adhered to the regimen.

DISCUSSION

Balance study. Departing from the common practice in collecting food samples for balance studies, duplicate portions of food for each meal were prepared (under supervision of the same dietitian) and weighed out. One portion was fed to the patient and the other placed in the refrigerator until the end of each period, when the samples were pooled, homogenized and a measured volume taken. To counteract bacterial activity, 10 cc concentrated sulfuric acid was added, and the material was analyzed for calcium, phosphorus and magnesium, as described, using the same scale. Thus variations in excretion products could be checked against actual food consumption.

The dietary values were calculated from Sherman's tables[15] (table 1). Although the mineral content of foods produced in different parts of the country are likely to vary, the findings for calcium and phosphorus in the study differed only slightly from the calculated values,[16] but the magnesium averaged 0.1 gm. less than the calculated figures.

On an average diet, normal excretion of calcium in the serum ranges from 9 to 11 mg. per cent in 24 hours; in the urine, from 100 to 200 mg.; and in the stool is 500 mg. per cent. (Ordinarily, 65 to 75 per cent of ingested calcium is excreted in the feces; and the remaining 25 to 35 per cent in the urine, although greater variations may occur.) For phosphorus the range is 3 to 5 mg. per cent in the serum, 300 to 500 mg. in the stool, and in the urine is approximately 1 gm. as inorganic phosphorus. For magnesium the range is 1.9 to 2.1 mg. per cent in the serum, 100 to 200 mg. in the urine, and two or three times as much in the stool.[17]

Unexpectedly, in this study, urinary calcium excretion was definitely low in the 3 experimental subjects, in comparison with normal excretion by the control.

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[14] Shorr, E., et al.: J.A.M.A., in press.

[15] Sherman, H. C.: Chemistry of Food and Nutrition. New York: The Macmillan Co., 1941.

[16] Sherman, H. C.: Calcium and Phosphorus in Food and Nutrition. New York: Columbia Press, 1947.

[17] Peters, J. A. and Van Slyke, D. D.: Quantitative Clinical Chemistry, vol. 2. Baltimore Williams & Wilkins, 1932.[17a] Ibid, vol. I, p. 908, 1946.

This finding contrasts sharply the observation by Flocks[18] and Riegel[19] of idiopathic hypercalcinuria in 50 to 60 per cent of patients with recurrent renal stone.

The values for urinary magnesium also were below normal in the 3 subjects of the balance study, but in view of the low intake this may not be remarkable. Although stool calcium values could not be obtained and the calcium equilibrium was not determined, urinary excretion of calcium probably was enhanced by the increased ingestion and absorption of magnesium during period 2. This would confirm the work of Tibbetts and Aub.[20] A possible absorption of 6.5 per cent of the magnesium ingested daily as amphojel with magnesium trisilicate would permit 118 mg. to be retained or excreted in the urine.[21]

With all 3 subjects and the control the results showed definite changes in phosphorus metabolism (fig. 1). Urinary phosphorus excretion was reduced 78 per cent within 6 days, and began to return toward normal within 2 days after cessation of therapy. Hence it is clear that decrease in urinary phosphorus with associated increase of phosphate in the stool can be produced with regularity in both normal and calculous subjects.

The presence of magnesium trisilicate apparently had no effect on phosphorus metabolism but did cause a small but significant rise in urinary calcium excretion, probably as a result of the rise in urinary magnesium.[20] Excretion of magnesium in the stool increased rapidly in period 2 when amphojel with magnesium trisilicate was administered, and continued to rise during the subsequent recovery period. This was expected because the daily intake of magnesium, including that in amphojel with magnesium trisilicate, a relatively insoluble compound amounted to 1.8 gm.

Because urinary calcium excretion was low in all 3 subjects but not in the control during the fore period, it might be expected that the magnesium excretion also would be low. On the other hand, the relatively low intake of magnesium may partially explain the low excretion of magnesium. Subsequent studies have shown, however, that in idiopathic hypercalcinuria, with or without amphojel therapy, urinary magnesium excretion is not high. An attempt to confirm the experimental evidence of Hammersten by correlating these findings with the type of stone (oxalate or phosphate) produced would be desirable.

If a high content of magnesium in the urine would increase the solubility of the calcium oxalate and maintain all the calcium in solution, it might prove valuable in therapy. Many so-called oxalate stones contain a nucleus of calcium oxalate, laminated, as a result of infection, with calcium phosphate and carbonate. A high urinary magnesium might then contribute to the growth of calcium phosphate and carbonate calculi, rather than increase the solubility of calcium oxalate. Nevertheless, for all stone-forming patients, it would seem advisable to provide a diet adequate in magnesium to reduce excretion of endogenous oxalic acid to a minimum.

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[18] Flocks, R. H.: Calcium and phosphorus excretion in the urine. J.A.M.A., **113:** 1466, 1939.

[19] Riegel, C., et al.: Chemical studies in hyperparathyroidism and urolithiasis. J. Urol., **57:** 192, 1947.

[20] Tibbetts, D. H. and Aub, J. C.: Magnesium metabolism in health and disease. J. Clin. Invest., **16:** 491, 1937.

[21] West, E. S. and Pennoyer, C.: Some effects of magnesium trisilicate ingestion upon blood urine and feces of human subjects. Am. J. Digest. Dis., **12:** 199, 1945.

Clinical findings. The satisfactory results obtained in prophylaxis of renal stone indicate the desirability of alumina gels for this purpose.

Inability to reduce urinary phosphorus excretion in the 4 who did not respond cannot be attributed in all cases to failure of therapy. In 2 of these, H. H. and S. (also a subject in the balance study), in whom stones recurred, determinations of urinary phosphorus excretion showed failure to take an adequate dosage. For H. H., in whom calculus enlarged, the daily excretion of phosphorus in the urine was never less than 346 mg.; the average value was 602 mg. S. had been maintained satisfactorily on plain amphojel, with average daily urinary phosphorus excretion of 0.271 gm. Previous to the balance study, however, the values for urinary phosphorus rose to 1 gm., indicating that she had secretly discontinued use of amphojel, and when she passed a recurrent stone through the left nephrostomy tube her urinary phosphorus was 1.113 gm. per 24 hours. Following a ureterolithotomy, E. A. had a left ureteral stricture which could not be adequately dilated, and hydronephrosis inevitably developed. Even though it was possible, in this patient, to maintain an average urinary phosphorus excretion of 361 mg. per 24 hours, two ureteral calculi formed just proximal to the stricture. Urinary obstruction, an age-old factor in the production of stone, in this case was responsible for recurrence.

J. B., the patient with idiopathic hypercalcinuria, was excreting more than twice the normal amount of calcium in the urine before amphojel was started. Stone recurred despite regulation of diet, administration of vitamin A and adequate dosage with amphojel with magnesium trisilicate. This may be considered the only true failure in the series.

SUMMARY

Administration of alumina gel causes reduction in urinary inorganic phosphorus and increases excretion of phosphate in the stool of both normal and calculous subjects.

Amphojel with magnesium trisilicate was administered, in doses of 30 to 45 cc 4 times daily, for 2½ years to 34 patients for prophylaxis of urinary calculi. In 30 (88.2 per cent) the treatment was successful, with no evidence of recurrence or of enlargement of existing stone.

Of 3 patients who did not adhere to the prescribed regimen, 1 showed stone growth and the other passed a stone through a nephrostomy tube. In a third, stones formed proximal to a ureteral stricture.

In a fourth patient, with idiopathic hypercalcinuria, recurrence was attributed to a high urinary calcium.

There was no evidence of decalcification of the skeleton or other ill effects in any of the patients studied.

Observations on 2 uremic patients suggest that diversion of the phosphate through the gut, thus partially relieving the kidney of the necessity to excrete

phosphorus, may be of therapeutic value in uremia by facilitating excretion of urea, with reduction of serum urea nitrogen.

Ten patients who had received amphojel with magnesium trisilicate previously were treated with basaljel, an aluminum carbonate gel, in the same dosage. It reduced urinary phosphorus excretion to lower levels than did plain amphojel or amphojel with magnesium trisilicate, and is more palatable. Basaljel, therefore, appears to be the drug of choice for prophylaxis of calculi in the urinary tract.

In the balance study urinary magnesium paralleled urinary calcium in the 3 subjects and the control.

Urinary calcium increased slightly on amphojel with magnesium trisilicate but not with plain amphojel.

Positive balances in phosphorus and magnesium metabolism were maintained during alumina gel therapy.

Since earlier experiments suggest that a high urinary magnesium may increase solubility of the calcium oxalate and maintain all calcium in solution, an attempt to confirm these findings would be desirable.

It appears advisable, for stone-forming patients, to provide a diet adequate in magnesium to reduce endogenous oxalic acid excretion to a minimum.

The author expresses gratitude to Dr. George F. Cahill, director of Squier Urological Clinic, for his kind cooperation and financial assistance; to Dr. Alexander B. Gutman, who furnished laboratory facilities; to Miss Lottie Fogel and Mrs. Blanche Markardt for their services in developing and determining the chemical methods; to Mrs. Rose Yager, who carried out the chemical determinations during the last year and aided in compilation of the data; to Miss A. Cowan, dietitian in charge throughout the balance study; and to Mrs. I. Waters and Miss M. Susanin, of the food clinic, who prepared the maintenance diets.

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TRAUMATIC RENAL INFARCTION CONCURRENT WITH MASSIVE FAT EMBOLISM

GORDON M. CARVER, JR.

The occurrence of traumatic infarction of the kidney associated with massive fat embolism is so rare that it warrants reporting 2 cases recently observed by the author. Traumatic infarction of the kidney has been infrequently reported, only 4 cases being found in the literature. In Aschner's review of renal infarctions, von Recklinghausen is quoted as reporting the autopsy of an 8 year old boy who died 8 days after a severe fall. The left renal artery showed a circular injury of the wall. Distal to this there was extensive thrombosis of all branches. and there was complete necrosis of the kidney. Barney and Mintz, in their study of the Massachusetts General Hospital protocols, found a similar instance of a man, who died 8 days after a fall on his back. At autopsy a large infarct was found secondary to thrombosis of practically all of the vessels of the kidney. Hirshberg and Sall reviewing the literature on renal infarction involving 376 cases, found the above mentioned 2 cases, and added a third case of their own. Rexford and Connolly reported the fourth case in 1945.

The clinical picture of traumatic infarction of the kidney is similar to that of ruptured kidney; with pain, shock, localized tenderness, macroscopic hematuria, and the findings of a mass in the flank, following a history of trauma to the renal area.

The excretory urogram reveals the absence or diminished function of the involved kidney. Retrograde pyelograms show an intact kidney pelvis. The history is of value in differentiating renal infarction of a traumatic nature from that secondary to cardiac disease, which constitutes the great majority of the cases.

The prognosis is favorable when there is uncomplicated unilateral involvement, and if operation is performed early in severe lesions. If gross hematuria persists for more than 24–48 hours, the renal area must be explored; not only to rule out the possibility of severe exsanguinating bleeding from a ruptured kidney, but to perform a nephrectomy if the kidney is severely damaged by infarction.

The gross pathology of the infarcted traumatized kidney reveals it to be slightly enlarged and edematous. The renal capsule and pelvis usually are intact. In the cortical areas large yellowish-gray, irregular, triangular infarcts are seen, and usually gross damage to the renal vessels, can be demonstrated. Microscopically one sees various stages of necrosis. Hemorrhage is seen throughout the tissue and thrombi are found in numerous vessels. A widespread anemic type of infarction is seen limited to the cortex, and separated from the medulla by a wide barrier of hemorrhage, infiltration of polymorphonuclear leukocytes, and plasma cells.

FAT EMBOLISM

Fat embolism as a clinical entity has been known since 1862 when Zenker observed the first fat emboli in the pulmonary capillaries of a railroad worker following a severe crushing injury. As early as 1880, Scriba was able to collect 177 cases from the literature and add 34 of his own. Since that time, more than 650 known references to fat embolism are to be found in the literature, yet it is sufficiently rare that in civilian practice the diagnosis is entertained antemortem infrequently.

Fat embolism is usually associated with trauma of a physical or chemical nature, and access to the vascular system as proposed by Milosalvich is through ruptured veins. Gauss pointed out that fat embolism was more common in fractures than in any other condition, because the veins, being encased in a bony wall, are noncollapsible remaining open for the admittance of fatty substances, which occurs as soon as hemorrhage and exudation develops about the fracture site, raising the local pressure above that of the venous pressure. Fat embolism following extensive trauma to soft parts, such as in bomb explosions or burns, is somewhat more difficult to explain, but in marked concussions the extensive disruption of the adipose tissues will very easily force fat into the circulation; and in the case of burns, the death of fat cells in the panniculus may liberate fat, and local edema, beneath an eschar or pressure bandage will tend to force the fat into the capillary or venous circulation. (Warren.)

The incidence of fat embolism varies a great deal according to the various reports. Darrach reported 2 cases of fat embolism among 12,000 fractures treated at the Presbyterian Hospital in New York. Grondahl reported 1 case of fatal cerebral fat embolism among 1,029 fractures. Wilson and Salisbury reported 8 cases among 1000 battle casualties of World War II. Robb-Smith studied 789 consecutive bombing accidents, of which 125 were fatal. Forty-one of the fatal cases showed gross pulmonary fat emboli. Wakeley found fat embolism present to varying degrees in 40 per cent of his fatally burned cases, Warren, in studying 100 cases of fatal fat embolism, found that 82 per cent had fractures of the femur, tibia, or both, either alone or combined with fractures of other bones. Fat embolism should be expected in every severe case of fracture of the long bones of the lower extremity and the embolic occurrence rate would be astounding in this group of fractures. There have been 3 cases of fat embolism on the Orthopedic Service at the Johns Hopkins Hospital in the past 3 months in patients with fractures of the lower extremities.

The normal blood fat varies from 0.6 to 0.7 per cent, and in diabetic coma the total blood lipid may be 18–26 per cent; however death from fat embolism in diabetic coma is rare, because the chylomicronous globules are less than 12 μ. in diameter and will go through pulmonary capillaries. (Boyd.) The size and chemical state of these embolic fat particles are of principal importance, and therefore blood chemical lipid determinations are of little clinical value.

The gross and microscopic pathological evidences of fat embolism vary according to the severity and duration of the phenomenon. In the acute case with massive embolism and early death, pulmonary edema is usually present, perivascular petechial hemorrhages throughout the brain can be seen, and fat globules can be demonstrated in pulmonary and renal tissue. In the chronic cases pulmonary consolidation, in addition to hemorrhage, and edema are present;

small foci of softening surrounded by a hemorrhagic zone occurs in the brain tissue, and petechial hemorrhages may be demonstrated in the pericardium, conjunctivae, pleurae, and skin. It is difficult to perceive that an inert fat globule would cause the perivascular changes seen microscopically, and Hirsch pointed out that the reaction of tissues to unhydrolized fat was similar to that of inert oil-like liquid petrolatum, however hydrolysis of fat liberates fatty acids and other chemical bodies which presumably are responsible for the destruction of the vessel wall, and the perivascular pathological changes.

The clinical features vary according to the severity of the embolic phenomenon. Burger suggested three clinical forms: 1) the peracute, where death occurs in a few seconds, 2) the acute, where the symptoms appear immediately after injury, and death occurs in hours to days; 3) the subacute, where a free period occurs between trauma and the onset of symptoms. The majority of the cases are of the subacute type, and typically there is a history of trauma, usually with fracture of a long bone or severe soft tissue damage. The patient is treated for shock and reduction of fracture is accomplished under general anesthesia. After anesthetic recovery the patient is oriented and cooperative, and his pulse, blood pressure, and respiratory rate are normal. The asymptomatic period may last 6–72 hours; however the patient soon becomes apprehensive, develops tachypnea, tachycardia, hyperthermia, and hypertarachia. The clinical signs, once initiated, are usually progressive: and respiratory embarrassment may increase to cyanosis, deep stertorous breathing, and often Cheyne-Stokes respirations in the terminal stages. There may be pain in the chest with auscultory signs of consolidation, and x-ray of the chest reveals diffuse increase in density of both lung fields.

The pulmonary arterial pressure increases, there is a compensatory tachycardia, and as the pulse becomes faster and stronger, the blood pressure begins to rise.

The temperature is usually high, ranging from 102–107, depending on whether or not the heat regulating center is involved by the emboli.

The involvement of the central nervous system is further manifested by changes in the state of consciousness, loss of sphincter control, muscular rigidity, convulsions, and sometimes Jacksonian fits.

Petechial hemorrhages may appear in the skin but their number seems to have no relation to prognosis. The most common site of occurrence is about the neck and the inferior half of the conjunctiva.

Fundiscopic examination may reveal retinal fat globules, as first reported by Oppenheimer in 1929, but more typical are pathological changes in the substance of the retina itself, consisting of yellowish-white glistening patches of perivascular edema, or patches of perivascular hemorrhage.

The diagnosis of fat embolism must be made primarily from the history, clinical signs, and symptoms. The examination of the sputum, blood, and lung puncture are not conclusive. Fat in the urine is more significant, but is difficult to demonstrate, and does not usually appear until the third or fourth day in the course of the disease. It is important to remember that fat in the bladder floats on top of the urine, and is best obtained by catheterization after voiding, or by catching the last few drops of voided urine separately. The fat can then be demonstrated by Sudan III stain, or perhaps the "Sizzle Test," described by Scuderi may be of value.

The treatment of fat embolism is nonspecific and consists mainly of symptomatic therapy. Preventive treatment includes protection from post-fracture trauma by proper splinting, and early evacuation of local hematoma, on the theory that local tension increases the liability of fat to enter the venous sinuses. Von Klapp (1931) ligated the femoral vein, and various substances have been injected intravenously without significant benefit. A specific therapeutic agent for the treatment of fat embolism remains obscure.

DISCUSSION

Traumatic renal infarction when associated with fat embolism merely adds the clinical findings of gross hematuria, decreased or absent renal function on the involved sides, the finding of a perirenal mass, and shock, to an already complicated clinical entity which is not well known. Conservative treatment is advised unless macroscopic hematuria persists beyond 24–48 hours, or blood loss is so severe as to force operation. If the hematuria is due to the infarction, it usually subsides in 48 hours.

The question arises as to whether the infarction present in these cases presented might not be due to the fat embolism. Warren reviewed 100 cases of fatal fat embolism and reported no such lesions. In fact he was amazed that the renal glomeruli did not show evidence of damage even when there was virtually complete occlusion by fat of the afferent arterioles, as well as all of the capillaries in the glomerular tufts. Both of the cases presented here had severe trauma to the renal area with fracture of transverse processes, and overlying ribs, and at autopsy huge ischemic infarcts were found, some measuring 3 cm. in diameter.

CASE REPORTS

W. R., a 23 year old Negro, was brought into the Johns Hopkins Hospital accident room at 1:15 a.m. on February 26, 1950 by police officers, who found him lying by the side of the Cockeysville highway, after having been hit by an auto. The patient was oriented, but unable to relate any details of the accident.

Physical examination revealed a well developed and nourished Negro who was oriented as to time, place and person, but who was in obvious acute distress with bilateral compound, comminuted fractures of the tibia and fibula. The odor of alcohol was detected from the patient's breath. There was a superficial abrasion and laceration of the right scalp; examination of head and neck was negative. Lungs were clear to percussion and auscultation, although there was some splinting of the right thorax on inspiration. The heart was not enlarged, and there was no murmur. Pulse 110, respirations 24, blood pressure 132/80. The abdomen was soft with slight tenderness in the right upper quadrant and in the right costovertebral angle. Marked tenderness was also noted on the right over T12, L1, L2, L3. The upper extremities were not injured. Over the anterior midportion of the right lower leg one could see a large cutaneous defect, from which protruded a 4 inch piece of fibula attached only by a sliver of periosteum. Several loose pieces of tibia lay free in the severely contused and solid wound. Particles of leaves and gravel could be seen imbedded in the soleus muscle belly. The right anterior tibial artery and nerve were intact, although pulsations were poorly felt. The left lower leg had two small puncture holes 2 cm. in diameter in the skin overlying the fracture site in the anterior tibial region. Peripheral pulse was easily palpable in this extremity. Neurological examination was entirely negative. Pupils were equal and responded to light and accommodation. There was no hemorrhage or exudate noted over retina. Optic discs were clearly outlined, and no conjunctival petechia were present.

It was obvious from physical examination that the patient had bilateral compound comminuted fractures of both tibias and fibulas with associated traumatic renal disease. Catheterization revealed grossly bloody urine. The patient was given 500 cc plasma and x-rays of the chest, legs, pelvis, abdomen, and an excretory urogram were taken. X-rays revealed marked fragmentation of bones at the fracture site bilaterally. The lungs were clear; the excretory urogram revealed no excretion of dye from the right kidney, and very minimal excretions from the left; the abdominal film revealed fractures of L1, L2, L3, L4 transverse processes and the twelfth rib on the right side.

The patient was carried to the operating room immediately where extensive irrigation and débridement were performed. The left tibia was fixed with a Lane plate, and the right tibia fixed with Steinman pins placed well above and below the fracture site, and incorporated in a full leg case. The patient received 1000 cc of blood during the operative procedure, and was never in shock. He responded readily from the pentothal sodium anaesthesia and was able to eat a light lunch at 12 noon. Tetanus antitoxin and gas bacillus antitoxins were administered.

The first postoperative day was uneventful; however the next day he began to have transient episodes of disorientation and tachypnea. A lumbar puncture was performed and the patient placed in an oxygen tent. Spinal fluid pressure (initial) was 220 mm. H_2O. *Pandy* negative. Cells 350 crenated red blood cells without xanthochromia. Ratio of 10 1 crenated normal. Six white blood white cells, 90 per cent polymorphonuclears. The urine which had been grossly bloody on admission was now light pink. An excretory urogram revealed no function of right kidney and diminished output of the left kidney. The urinary output first 24 hours was 600 cc and second 24 hours 1310 cc. The patient failed to improve in the next 48 hours, and remained restless, semi-comatosed, and refused oral feeding. Blood 500 cc was given, and blood chemistry revealed a nonprotein nitrogen of 62 mg. per cent. Retrograde pyelograms revealed no distortion of the calyceal systems. No blood was present in the urine at the time of retrograde pyelography. On the sixth postoperative day the patient had a shaking chill followed by a temperature of 107F. A blood culture was drawn and x-ray revealed lungs to be clear. The patient's hyperthermia responded to alcohol sponge baths, but he became disoriented, blood pressure dropped to 100 60 from 190 110 prior to chill, respirations became extremely rapid and irregular, and the patient expired on the eighth postoperative day. (See fig. 1

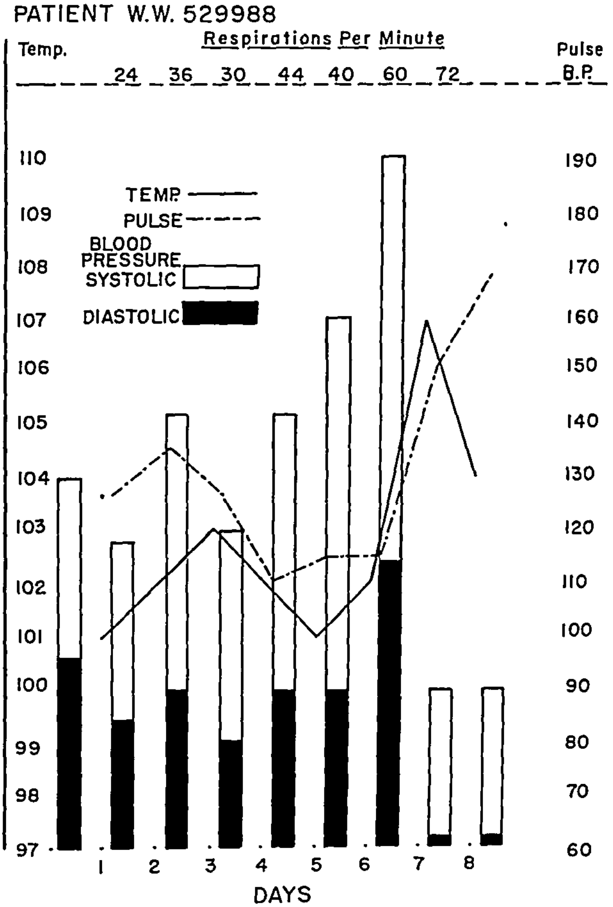

Fig. 1.

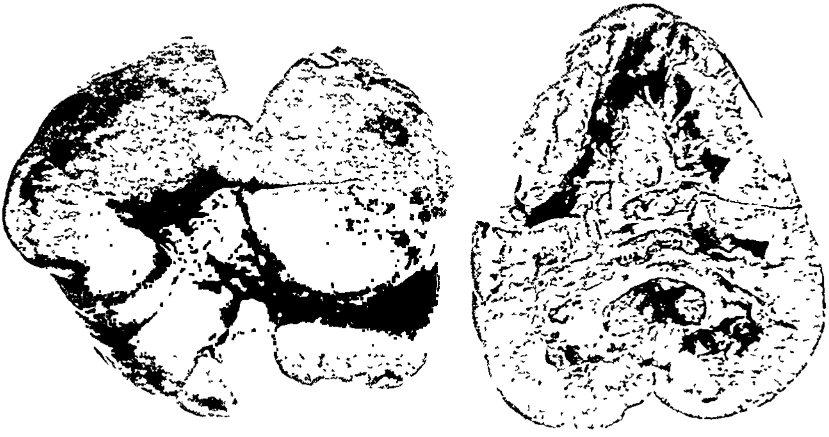

Fig. 2. Case 1. Right and left kidney showing huge yellowish-gray, ischemic, traumatic infarcts in renal cortical area. Largest measured 3.5 by 1.5 cm

for average of daily pulse, respiration, blood pressure, and temperature during hospitalization.)

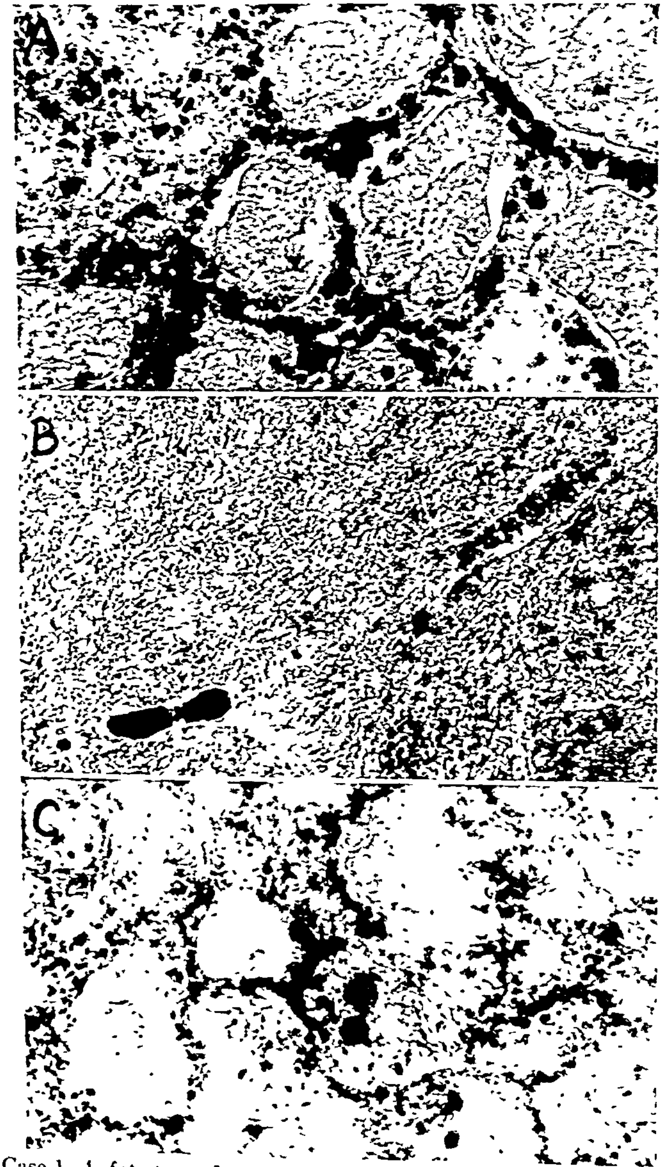

FIG. 3 Case 1 *A*, fat stain of renal cortical area. Note numerous fat globules, stained black, in peritubular vessels, and occasional globules in afferent glomerular vessels. × 300 *B*, fat embolus occluding cerebral blood vessel × 300 *C*, pulmonary fat embolism showing fat in edematous alveoli and capillaries. (Black staining particles) × 300.

At autopsy the kidney revealed two distinct processes; fat embolism, and anemic infarction limited to the outer cortex (fig. 2). This fat was present mainly in the glomeruli and peritubular vessels (fig. 3, *A*). The brain showed multiple foci

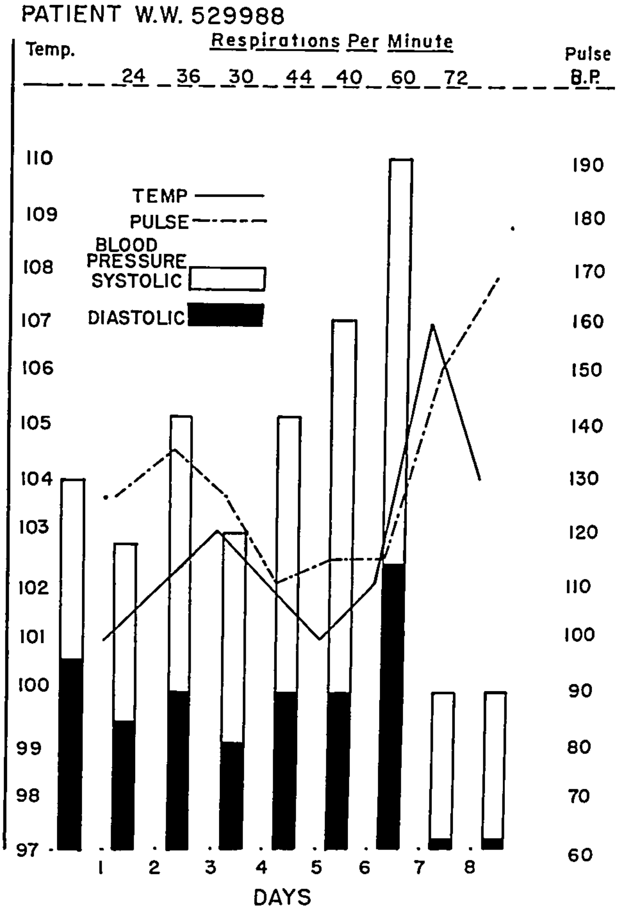

Fig 1

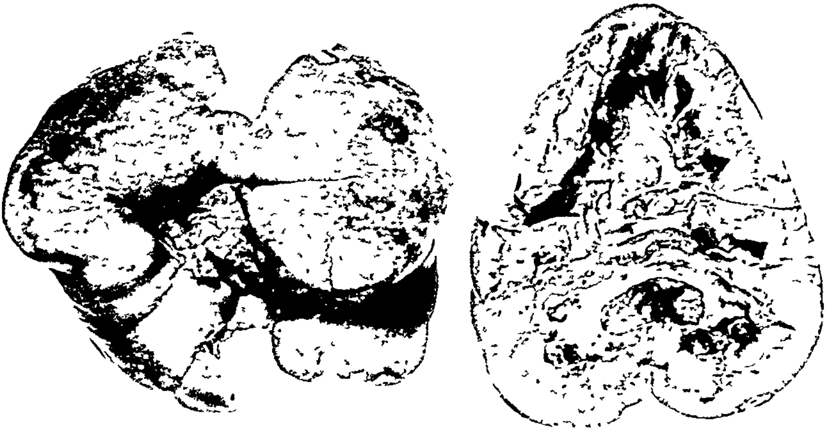

Fig. 2 Case 1 Right and left kidney showing huge yellowish-gray, ischemic, traumatic infarcts in renal cortical area Largest measured 3 5 by 1 5 cm

for average of daily pulse, respiration, blood pressure, and temperature during hospitalization.)

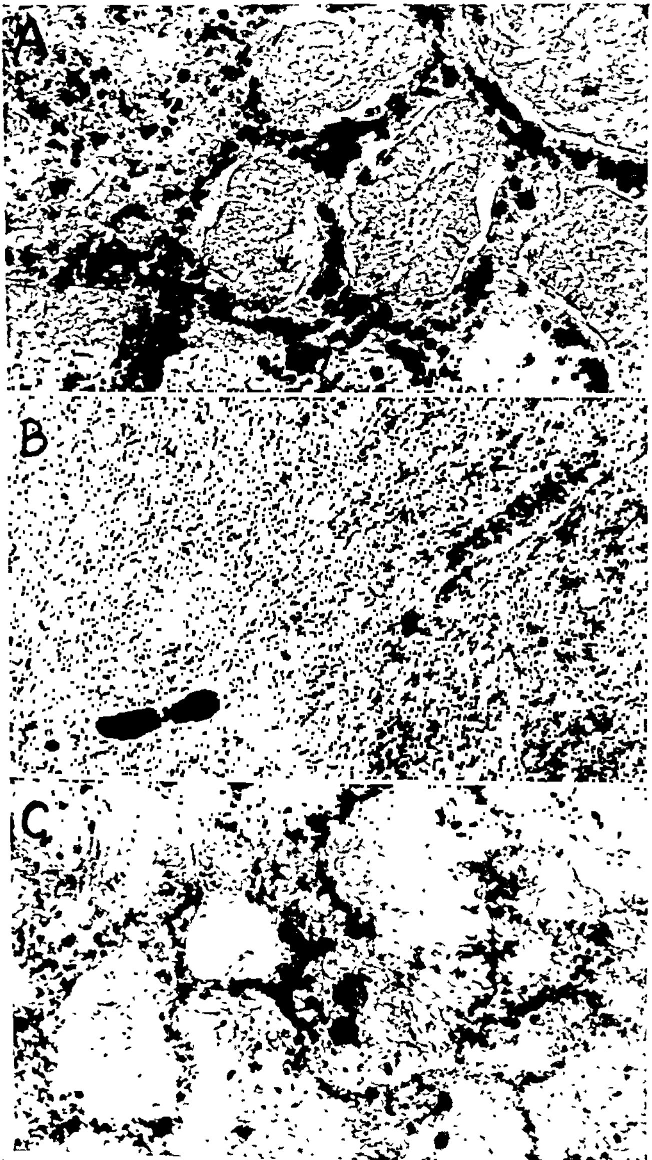

FIG. 3. Case 1. *A*, fat stain of renal cortical area. Note numerous fat globules, stained black, in peritubular vessels, and occasional globules in afferent glomerular vessels. × 300 *B*, fat embolus occluding cerebral blood vessel. × 300. *C*, pulmonary fat embolism showing fat in edematous alveoli and capillaries. (Black staining particles.) × 300.

At autopsy the kidney revealed two distinct processes; fat embolism, and anemic infarction limited to the outer cortex (fig. 2). This fat was present mainly in the glomeruli and peritubular vessels (fig. 3, *A*). The brain showed multiple foci of perivascular hemorrhage and necrosis. Many capillaries were distended with hyalin thrombi and others with exudate. Fat stains revealed diffuse fatty degenerative changes in the parenchyma, and occasional globules of fat in capillaries (fig. 3, *B*). A hemorrhagic edema was seen throughout the lungs and fat stains showed many globules present in the capillaries (fig. 3, *C*).

Case 2. H. B. (537698), a 68 year old Negro, was admitted to the Johns Hopkins Hospital accident department soon after being hit by an auto. He was oriented and never lost consciousness, but impending shock was evident, and he was given 1000 cc whole blood, and 500 cc plasma.

Physical examination and x-ray studies revealed the following fractures: 1) Linear fracture of the right frontoparietal region; 2) transverse fracture through the body of the left mandible; 3) fracture of the right second rib posteriorly; 4) comminuted fracture of the left midhumeral shaft; 5) transverse fracture of the left fifth rib; 6) comminuted fracture of the right glenoid; 7) multiple rib fracture in the paravertebral region bilaterally, T8, T12; 8) avulsion fracture of the left medial femoral condyle; 9) fracture of the left tibial plateau. The lungs were clear to percussion and auscultation. The heart was not enlarged, rate and rhythm regular. Blood pressure, 100/60, pulse 100, respirations 30. The abdomen was soft without masses. Urinalysis revealed grossly bloody urine, and an excretory urogram performed 12 hours later revealed no excretion of dye.

The patient was admitted to the hospital emergency ward immediately, a cast was applied to the left arm, a Barton dressing to support the mandible, and a protective dressing to the left knee with direct traction applied to the left foot. A slight drop in blood pressure to 100/60 was soon noted with associated dyspnea. The patient was placed in an oxygen tent, and given 600 cc blood with a temporary response. His temperature soon rose to 103.4F however, and his subsequent course was rapidly terminal.

The patient was anuric for 18 hours after which his urine was grossly bloody; but cleared before death, which occurred 36 hours after admission.

The post mortem examination revealed: 1) Multiple abrasions, contusions, and fractures as previously listed; 2) rupture of lung, liver, and right kidney, upper pole; 3) fibrinous pleurisy, right and pericarditis; 4) multiple fat embolism, fat being demonstrated microscopically in the lungs, kidney and brain; 5) traumatic infarcts of the kidney, right.

SUMMARY

Two cases of traumatic infarction of the kidney associated with massive fatal fat embolism are presented.

Review of the literature regarding traumatic infarction of the kidney, and fat embolism as separate entities is presented.

Fracture of the long bones of the lower extremity should immediately suggest the possibility of fat embolism, and renal trauma associated with hematuria should suggest the possibility of renal infarction.

Traumatic infarction of the kidney should be treated conservatively when possible.

Renal pathological damage following even massive fatal fat embolism is remarkably benign.

Duke Hospital, Durham, N. C.

REFERENCES

Aschner, P. W.: Am. J. Med. Sc., 164: 386, 1922.
Barney, J. D. and Mintz, E. R.: J. A. M. A., 100: 1, 1933.
Hirshberg, H. A. and Soll, S. N.: J. A. M. A., 119: 1088, 1942.
Rexford, W. K. and Connolly, P. J.: Am. J. Surg., 68: 259, 1945.
Zenker, P. A.: Beitr. z. norm. u. path. Anat. d. Lunge. 1862.
Scriba, J.: Deutsche Ztschr. f. Chir., 12: 118, 1880.
Miloslavich, E. L.: Wisconsin M. J., 29: 139, 1930.
Gauss, H.: Arch. Int. Med., 18: 76, 1916.
Warren, S.: Am. J. Path., 22: 69, 1946.
Darrach, W.: Discussion of: Harris, R. I., Perrett, T. S. and MacLachlin, A., Ann. Surg., 110: 1113, 1939.
Grondahl, N. B.: Deutsche Ztschr. f. Chir., 111: 56, 1911.
Wilson, J. V. and Salisbury, C. V.: Brit. J. Surg., 31: 384, 1943–44.
Robb-Smith, A. H. T.: Lancet, 1: 135, 1941.
Wakeley, C. P. G.: Surgery, 10: 207, 1941.
Boyd, E. M.: J. Biol. Chem., 101: 323, 1933.
Hirsch, E. F.: Arch. Path. & Lab. Med., 31: 516, 1941.
Burger, L.: Med. Klin., 11: 996, 1915.
Oppenheimer, H.: Klin. Wochenschr., 8: 24, 1929.
Scuderi, C. S.: Surg., Gynec. & Obst., 72: 732, 1941.
Klapp, R. Von: Zentralbl. f. Chir., 58: 2954, 1931.

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ELLIPTICAL END-TO-SIDE CONNECTION TECHNIQUE APPLIED TO REPAIR OF URETEROPELVIC JUNCTURE CONSTRICTION: A REPORT OF THREE CASES

WM. W. MILLER, JR., Lt. Comdr. (MC) USN

Hydronephrosis is not too uncommon a problem in the age group seen in the military. During a 12 months period, 12 cases were admitted to the urological serivce. Four of these cases were deemed correctable. In the remaining 8 cases the hydronephrosis was of such an extent there was no kidney substance left for salvage and nephrectomies were performed. One of the four in the group that could be corrected was done by the method of Heineke-Mikulicz; the other 3 were corrected by applying to the ureteropelvic junction the end-to-side elliptical connection technique described by Nesbit for uretero-intestinal anastomoses. The results in these 3 cases were so satisfactory it was believed that they merited reporting.

No attempt has been made to review and compare the merits of the many types of plastic operations described for the correction of difficulties at this point. Suffice it to say that the fact that many procedures exist for the correction of these difficulties speaks against 100 per cent success with any one method.

These cases are reported to add to our armamentarium another method for the correction of hydronephrosis resulting from some constricting factor at or near the ureteropelvic junction. To the best knowledge of the author this is the first group of cases handled in this particular manner.

A review of the causes and many types of pyeloplasties is not included because of their easy availabilty elsewhere. Because of the splendid results obtained with uretero-intestinal anastomosis and uretero-uretero-anastomoses by the end-to-side elliptical connection principle it seemed reasonable to apply it to corrective procedures at the ureteropelvic region. It is essentially the problem of a larger cavity emptying by a small caliber pipe; the uretero-intestinal situation in reverse. The simplicity of performance and uniformity of good results in the cases to follow speak in favor of wider dissemination of the procedure.

The patient is prepared in the usual manner for a kidney operation. General anesthesia is preferable. A straight flank incision is made to the transversalis muscle. Then the lumbodorsal fascia is nicked and the transversalis opened by blunt dissection with the thumbs, thus avoiding injury to the peritoneum (fig. 1). The ureter is located adherent to the peritoneal surface and carefully dissected to the renal pelvis after incising Gerota's fascia. The renal pelvis is also exposed. The constricted area of the ureter is located and any accessory vessels clamped, lysed and ligated. Then the ureter is severed from the renal pelvis. It is split longitudinally on its anterior surface for approximately 1½ cm., or until the strictured area is passed. A compatible incision is made in the renal pelvis at the

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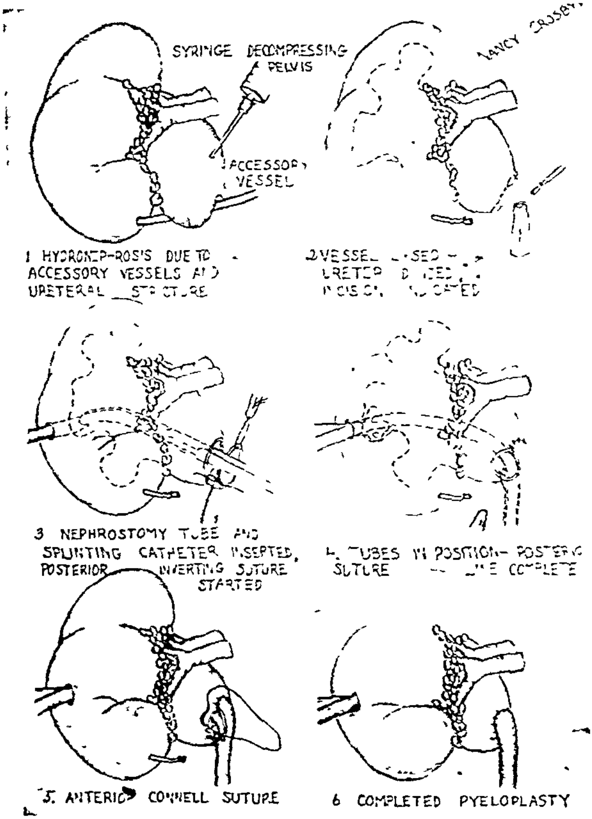
most dependent portion. If the original location of the ureter was not so located this rent is closed and a new opening made so it corresponds to the incision in the ureter.

At this time a nephrostomy is established by forcing a Kelly forceps through the kidney parenchyma by way of the opening in the pelvis. After calibrating the ureter, the largest urethral catheter (10, 12, 14F) it will comfortably accommodate is pulled into place with the Nesbit nephrostomy catheter. With the tubes in place the anastomosis of the ureter to the pelvis is carried out.



1 HYDRONEPHROSIS DUE TO ACCESSORY VESSELS AND URETERAL STRICTURE

2 VESSEL ...SED — URETER DIVIDED, INCISION LOCATED

3 NEPHROSTOMY TUBE AND SPLINTING CATHETER INSERTED, POSTERIOR INVERTING SUTURE STARTED

4 TUBES IN POSITION— POSTERIOR SUTURE — LINE COMPLETE

5 ANTERIOR CONNELL SUTURE

6 COMPLETED PYELOPLASTY

FIG. 1 Various stages in technique

Stay sutures with 0000 or 00000 atraumatic chromic material are placed at each end of the ureteral incision. The lowermost suture is used to make the medial surface of the anastomosis by a simple over and over inverting suture. Knots are tied within the lumen at both the superior and inferior angles. At this point the urethral catheter is inserted into the ureter for approximately 10 cm. With the catheter in place the lateral half of the anastomosis is carried out. An inverting, running Connell suture is used to close this side.

It is important at this point that the kidney be fixed by some type of nephropexy to assure dependency of the anastomosis. One Penrose drain is left in the wound and it is closed in the usual manner. Both the nephrostomy tube and splinting catheter are separately anchored to the skin with silk sutures.

After the seventh day when all sutures but the tube anchors are out the nephrostomy tube is carefully irrigated with solution G by gravity to help prevent crystalliferous encrustations on the tubes and stone formation. This is continued until the morning of the twenty-second day. During this period antibiotic therapy is given and the patient kept very well hydrated.

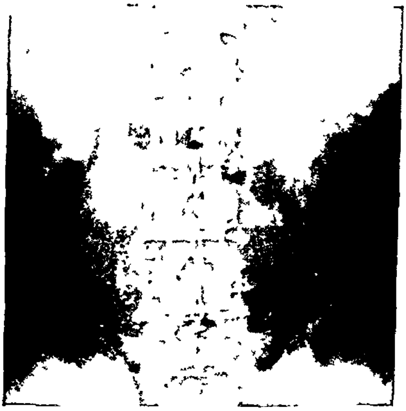


FIG. 2. Preoperative excretory urogram

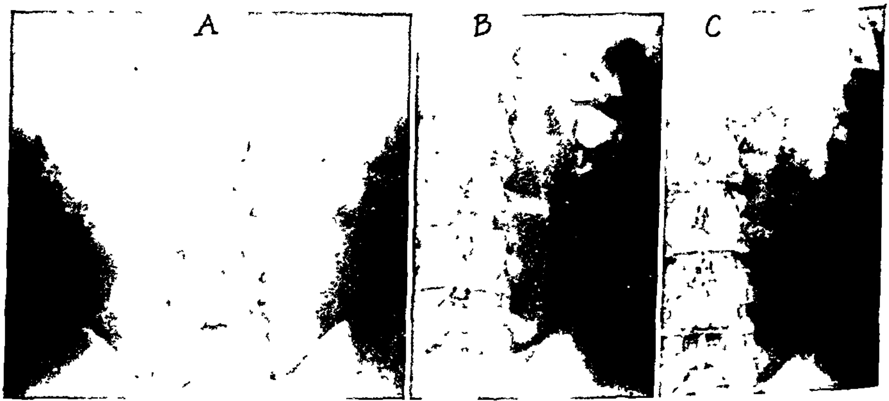


FIG. 3. *A*, preoperative excretory urogram showing 2 plus hydronephrosis. *B*, nephrostogram showing prompt filling of bladder. *C*, postoperative excretory urogram showing resolution of hydronephrosis.

On the twenty-second day the splinting urethral catheter in the ureter is removed through the nephrostomy wound which it extends. An injection pyelogram through the nephrostomy tube is made. The injection is made with the patient in the upright position and contrast medium introduced until the patient complains of a desire to urinate. In this way a good pyelo-uretero-cystogram is obtained and the patency of the new ureteropelvic junction tested. It is advisable to measure the amount of contrast medium injected and the time required for the desire to urinate to appear. A second film is taken in 30 minutes to determine the extent of dye retention in the pelvis. The nephrostomy tube is left in place, but clamped off completely for 3 days. An excretory urogram is then obtained with a 30 minute upright film. If the kidney pelvis drains promptly in the foregoing tests, the nephrostomy tube is removed. It is usual to experience rapid healing of the wound in 2 to 3 days. Check-up excretory urograms are

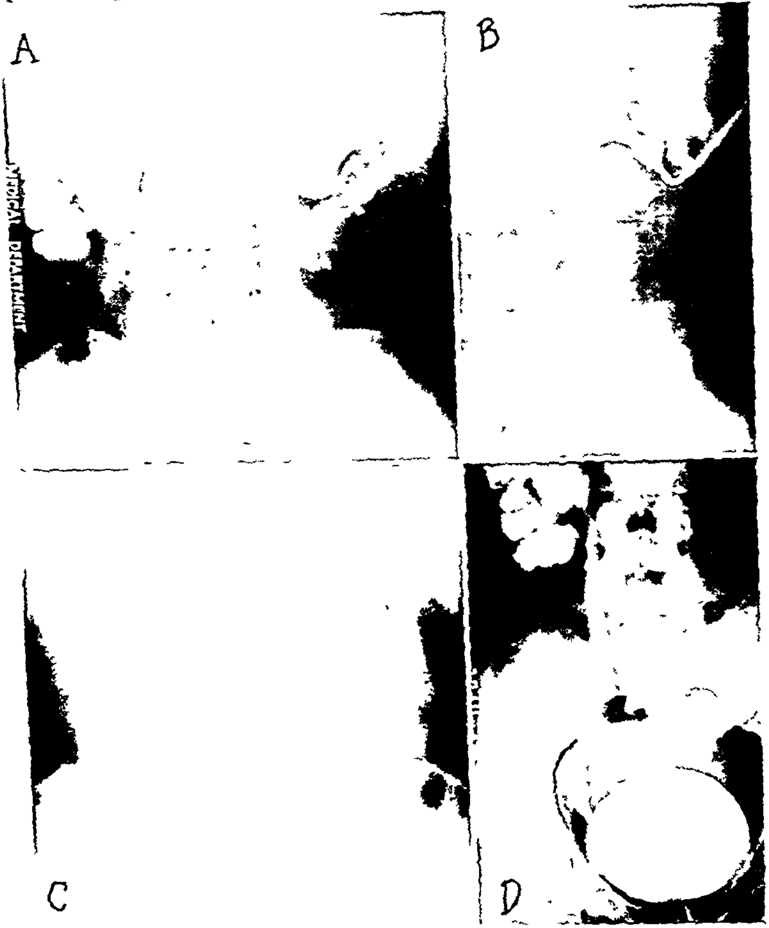


FIG. 4. *A*, preoperative *excretory urogram* showing bilateral hydronephrosis, more marked on right. *B*, left nephrostogram *showing* prompt dissipation of dye to bladder. *C*, postoperative excretory urogram showing *resolution of* left hydronephrosis. *D*, right nephrostogram showing adequate correction of obstruction.

advised after 6 weeks. The amount of resolution of the hydronephrosis depends upon the extent to which it had progressed before correction was undertaken.

CASE REPORTS

Case 1. W. J. M., a 26 year old white man, was admitted to the hospital complaining of dull left backache of 1 year's duration. Periodically more severe pains were noted. On physical examination the left kidney was palpable and costovertebral tenderness was present. There were no other significant findings. The urine was cloudy, contained clumps of white blood cells and cocci on stain. An excretory urogram demonstrated a normal right kidney and a 1 plus hydronephrosis on the left (fig. 2). On December 3, 1948 a pyeloplasty was done. An accessory artery and vein crossing the ureter to the lower pole of the kidney were found. These were divided. Convalescence was uneventful and a good result was obtained. The patient was discharged from the hospital on February 11, 1949. The postoperative urograms were excellent, but could not be located for publication.

Case 2. J. L. P., a 26 year old white man, was admitted to the hospital on September 10, 1948 as a tuberculosis suspect because of an infiltrative process in the left chest. This cleared completely during hospitalization. The physical and laboratory examinations were negative. On November 4, 1948 acute flank pain developed, which later became dull and chronic in nature. Urological studies demonstrated left hydronephrosis due to ureteropelvic obstruction (fig. 3, *A* and *B*). By March 14, 1949 tuberculosis had been ruled out and a plastic repair of the ureteropelvic abnormality accomplished. At operation an accessory vessel was found. Convalescence was uneventful. Urine examination one week after removal of the nephrostomy tube was normal. He was discharged from the hospital on April 21, 1949. Recheck pyelograms obtained in June 1949 showed a good result (fig. 3, *C*).

Case 3. F. P. K. a 29 year old white man, was admitted to the hospital on June 3, 1949 unaware of any illness but because he had been refused life insurance on the basis of his urinalysis. The physical examination and laboratory studies were all normal except the urine. It was cloudy, straw colored, acid, contained a trace of albumin, 2 to 3 red blood cells, 10 to 15 white blood cells, and no organisms on stain. Excretory urograms on June 7, 1949 demonstrated grade 1 left hydronephrosis and grade 3 right hydronephrosis with 2 small calculi in the right renal pelvis (fig. 4, *A* and *B*). Cystoscopy and retrograde studies confirmed these findings outlining abnormalities at both ureteropelvic junctures. On June 15, 1949 a left pyeloplasty was done with a splendid result. He was out of the hospital on July 16, 1949 for a period of convalescense. On August 6, 1949 he was readmitted for the right pyeloplasty which was done on August 8, 1949. Again the postoperative course was uneventful and a good result was obtained (fig. 4, *C* and *D*). Five weeks after discharge from the hospital his urine was normal on laboratory examination. The left hydronephrosis was due to an accessory vessel; on the right a congenital valve was found.

SUMMARY

The elliptical end-to-side connection principle has been successfully applied to obstructing lesions at the ureteropelvic junction.

The results in 3 cases handled in this manner have been shown.

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REFERENCES

Miller, W. W., Jr.: Ureterosigmoidostomy, experience with the Nesbit technique. U. S. Naval Bull., **49:** 1021–1032, 1949.

Nesbit, R. M.: *Ureterosigmoid anastomosis by direct elliptical connection:* Preliminary report. J. Urol., **61:** 728–734, 1949.

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DISCUSSION

DR. THOMAS D. MOORE (Memphis, Tenn.): Lieutenant Miller's presentation is of special interest because, in the elliptical end-to-side anastomosis of the split ureter to the renal pelvis, the procedure necessarily includes the complete severance of the ureteropelvic juncture which may be considered a violation of the time-honored principle that continuity of the ureter should be preserved whenever possible. Section of the ureter interferes with the neuromuscular mechanism of pelvio-ureteral peristalsis. Gruber demonstrated in 1928 "If a ureter which is contracting, either with peristalsis or antiperistalsis, is cut, the pacemaker continues to contract at the same rate while the dependent segment contracts much more slowly." The practical application of this physiologic observation is that the sluggish peristalsis of the ureter below the point of severance may be conducive to stasis and thus defeat the purpose of a plastic procedure.

On the other hand, the functional results in the three cases reported by Lieutenant Miller appear satisfactory and might be considered difficult to reconcile with Gruber's work, although the point of severance in these cases was at the ureteropelvic juncture whereas in the experimental work referred to the point of severance usually was in the midureter.

It has been my privilege to perform a similar type of pyelo-ureteroplasty on a boy 9 years of age who was a victim of bilateral hydronephrosis. Nearly four years before, a Y-type of pyelo-ureteroplasty had been performed on the right side which was followed by complete cicatricial stenosis at the site of the plastic. During the intervening period of 40 months a nephrostomy tube had been worn. On July 21, 1949 the kidney was explored, and the cicatricial stenotic segment, slightly more than a centimeter in length, was completely excised. The stump of the ureter was split for a distance of 1.5 cm. and anastomosed to an opening of similar length in the renal pelvis. The nephrostomy tube and splinting catheter were removed fourteen days later, followed by prompt closure of the sinus. Eight months later the lad was still clinically well. Only 12 cc could be aspirated from the renal pelvis, and there was a phenolsulfonphthalein output from this kidney of 10 per cent in 15 minutes. The pyelographic end result appeared satisfactory.

In another case the same type of elliptical mucosa-to-mucosa technique was used in a young woman on whom a left refluxing ureter was severed from the bladder and anastomosed to the opposite renal pelvis which lay at a lower level, both kidneys being ectopic in this case. The operation was performed September 5, 1947 and completely relieved the patient of frequently recurring attacks of severe pyelonephritis. Since then she has remained well, has gained 22 pounds in weight and is steadily employed. This case has been previously reported, but it represents another instance of the type of anastomosis described by Lieutenant Miller with the minor difference that in the two cases I am presenting the anastomosis was effected by a few interrupted sutures of fine catgut rather than by attempting a watertight anastomosis with continuous sutures.

Another point worthy of mentioning is that, in view of the rather generous ostium provided by this technique, it is doubtful that a splinting catheter is indicated. It is quite possible that the convalescence of these patients would have been just as satisfactory without nephrostomy drainage.

I wish to congratulate Lieutenant Miller on his very interesting presentation.

LIEUTENANT WILLIAM W. MILLER, JR. (Pensacola, Fla.): I wish to thank Dr. Moore for his kind discussion of the limited number of cases that I was able to present. I will reply to his remarks about the neuromuscular mechanism of the ureter and ureteropelvic junction in the following fashion: This organization in 1947 granted the first prize award to Dr. Jack Lapides of the University of Michigan for a splendid piece of work on the physiology of the ureter, and I believe, if we are to accept that concept, we can discount the previous work described in 1928 regarding a pacemaker in the pelvis such as we have in the heart musculature.*

Since that time, I have had the opportunity to remove kidneys in certain operations and fill the pelvis with 20 or 30 cc water and watch the ureter and the immediately removed kidney operate very nicely. I think that would demonstrate that the pelvis plays a very small part in the propulsion of fluid along the course of the ureter.

* Dr Lapides' work was done entirely on the intact human ureter and, therefore, could not properly be construed as refuting Gruber's observation. *Editor*

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SPINAL CORD INJURY: SOME UROLOGICAL ASPECTS

GEORGE C. PRATHER

Many papers have been published during the past few years on urological problems following spinal cord injury. Additionally, a monograph, as well as a technical bulletin from the Veterans Administration have recently described in some detail the physiological and clinical aspects incidental to this type of injury.

I cannot at this time relate any startling developments, but shall evaluate briefly the methods of treatment employed during and following the recent war and suggest possible avenues along which further progress may likely be found.

It has become evident that two requirements must obtain for continued progress in the study and advancement of the care of the urinary tract following spinal cord injury. First, a sufficiently large number of patients must be studied so that one may learn to distinguish between those patients who show normal progress and those who do not. Second, those in charge of groups of patients must be eager to achieve optimum results and must have the opportunity to deliberate thoughtfully on possible ways to explain and correct disabilities which do not follow the normal line of recovery. The aid of neurosurgeons will be required to accomplish and interpret effectively the blocking of various nerve trunks. The urologist will be required to devise or refine methods to determine tissue resistance at various segments of the urethra.

To review briefly the progress in the care of patients with spinal cord injury during the past fifteen years, we, as urologists, must pay tribute to a man who, even before the recent war, was able to effect a degree of rehabiliattion which seemed phenomenal to many of us. I refer to Donald Munro of Boston. Having known Munro personally and professionally for years, having great respect for his neurosurgical judgment in traumatic problems, and admiring his verbal felicity which can sear to a crisp or acclaim with stunning brilliance, I became intrigued with the opportunity to study the urological aspects of spinal cord injuries during the war. Despite the necessity of following orders in the Army, urologists did find opportunities to check on Munro's ideas. After careful studies some men in military service verified Munro's dicta. They also were intent, however, to equal or excel his results by other methods if possible.

At present, I see Munro's patients for consultation, urological study and evaluation when they have complications. Assuredly, he knows much more neurosurgery than I, but I may know a little more urology than he (although he might take exception to this latter statement). I cite him as the one who initiated the idea of rehabilitation which served as the impetus for the rest of us.

A sufficient number of spinal cord injuries occurred during the war to make possible the establishing of predictable patterns of recovery for injuries at

Read at meeting of New York Society, American Urological Association, New York, N. Y., April 19, 1950

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Read at meeting of New York Society, American Urological Association, New York, N. Y., April 19, 1950 various levels and of various extent. As a result of these studies, it became advisable to distinguish between the physiologically complete and the physiologically partial injury at a certain level. Semans recently emphasized the need for this differentiation in diagrammatic form, and Bors in his excellent bulletin stressed the separation of the complete and incomplete lesion.

We all realize that there will be exceptions to the normal path of recovery, problems which severely tax our thought and skill, but this realization should not disturb our concept of the usual physiological results.

In order to review briefly a diagrammatic type of concept of the physiological aspects which appear pertinent, I shall describe three stages of recovery which should eventuate (fig. 1). Each of the three stages can be clearly demonstrated only by numerous cystometric studies which reveal that progress from one stage to another is gradual. Without comparative data over a period of weeks or months, cystometric readings may be difficult to interpret.

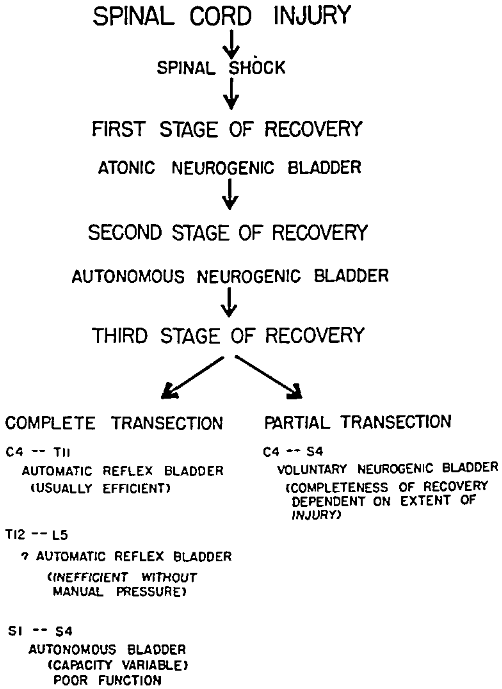

FIG. 1. Diagrammatic illustration showing stages of recovery of bladder following spinal cord injury. Some patients never progress beyond first or second stage. Some patients with complete transection C4–T11 pass through a hypertonic phase between second and third stage.

Immediately following spinal cord injury and during the period of "spinal shock," there is the loss of detrusor reflex. If the bladder is not put on drainage immediately, it distends and an atonic type of cystometric reading is apparent. (The term "atonic neurogenic bladder" is used in such an instance.) If the bladder is put on drainage before distention takes place, the intrinsic power of the bladder wall appears to be maintained to a better degree, exhibiting a gradually higher intracystic pressure with increased filling, I call this development the "first stage of recovery." In rare instances no further progress occurs.

In a variable period of time (days, weeks or months), a return of reflex activity becomes evident with cystometric study. This activity is demonstrated by a gradually rising intravesical pressure as the bladder is filled and by minor reflex contractions believed to be due to the nerve mechanism within the baldder wall. These reflex contractions are inadequate, however, to empty the bladder of its contents. The term "autonomous cord bladder" is applied to this phase which has been called the "second stage of recovery."

Obviously, further recovery to the third or final stage is greatly to be desired and will be manifested in various ways depending upon the level of the injury and its extent. If attainment of the third stage prevails, several subdivisions must therefore be considered.

First, the patient with complete transection of the cervical or thoracic segments down to the level of T11 should eventually develop and show efficient reflex bladder contractions which are presumed to be activated by a reflex arc from the bladder to the spinal cord below the level of the injury. A sustained reflex contraction of at least 70 cm. of water is required for periodic efficient voiding, usually at capacities of 150–400 cc of urine. The term "automatic reflex bladder" has been used for this type of vesical activity.

Second, the patient with complete transection at the level of T12–L5, sometimes referred to as conus lesions, may or may not develop reasonably efficient reflex contractions of the bladder, but often emptying of the bladder can be facilitated only by manual pressure on the lower abdomen at the time of reflex contraction.

Third, a patient with complete transection of the cauda equina (segments of S1–S4) has little chance of developing an automatic reflex bladder. The final cystometric chart may remain similar to charts made in the second stage of recovery, be they of an atonic or of a hypertonic type. I do not know the cause for this variability, but inefficient reflex activity is confined to the nerve mechanism within the bladder wall.

Fourth, the final stage of recovery in patients with partial transection of the cord; namely, those who have voluntary motor power and sensory appreciation below the level of the lesion should show a normal cystometric chart with efficient *voluntary* voiding. This type of bladder might well be called a "voluntary neurogenic bladder". Bladder capacity will be normal to increased, with bladder residual variable.

During the period of time in which the various stages of recovery should develop, the problems of maintaining the health of the patient, the flow of urine, the control of urinary infection, the integrity of the upper urinary tract, and the avoidance of wet beds or chairs require consideration. The present discussion is confined to the care of the bladder, a topic which is not likely to lead to unanimous agreement or conclusion.

Injuries incurred in civilian life might well be viewed in a different light from injuries sustained in war. In civilian life there is easy and rapid transportavarious levels and of various extent. As a result of these studies, it became advisable to distinguish between the physiologically complete and the physiologically partial injury at a certain level. Semans recently emphasized the need for this differentiation in diagrammatic form, and Bors in his excellent bulletin stressed the separation of the complete and incomplete lesion.

We all realize that there will be exceptions to the normal path of recovery, problems which severely tax our thought and skill, but this realization should not disturb our concept of the usual physiological results.

In order to review briefly a diagrammatic type of concept of the physiological aspects which appear pertinent, I shall describe three stages of recovery which should eventuate (fig. 1). Each of the three stages can be clearly demonstrated only by numerous cystometric studies which reveal that progress from one stage to another is gradual. Without comparative data over a period of weeks or months, cystometric readings may be difficult to interpret.

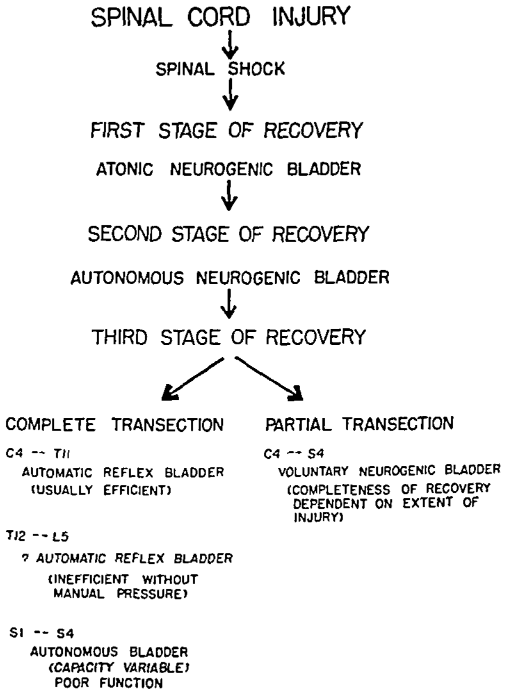
SPINAL CORD INJURY
SPINAL SHOCK
FIRST STAGE OF RECOVERY
ATONIC NEUROGENIC BLADDER
SECOND STAGE OF RECOVERY
AUTONOMOUS NEUROGENIC BLADDER
THIRD STAGE OF RECOVERY
COMPLETE TRANSECTION
PARTIAL TRANSECTION
C4 -- T11
AUTOMATIC REFLEX BLADDER (USUALLY EFFICIENT)
C4 -- S4
VOLUNTARY NEUROGENIC BLADDER (COMPLETENESS OF RECOVERY DEPENDENT ON EXTENT OF INJURY)
T12 -- L5
? AUTOMATIC REFLEX BLADDER (INEFFICIENT WITHOUT MANUAL PRESSURE)
S1 -- S4
AUTONOMOUS BLADDER (CAPACITY VARIABLE) POOR FUNCTION

FIG. 1. Diagrammatic illustration showing stages of recovery of bladder following spinal cord injury. Some patients never progress beyond first or second stage. Some patients with complete transection C4–T11 pass through a hypertonic phase between second and third stage.

Immediately following spinal cord injury and during the period of "spinal shock," there is the loss of detrusor reflex. If the bladder is not put on drainage immediately, it distends and an atonic type of cystometric reading is apparent. (The term "atonic neurogenic bladder" is used in such an instance.) If the bladder is put on drainage before distention takes place, the intrinsic power of the bladder wall appears to be maintained to a better degree, exhibiting a gradually higher intracystic pressure with increased filling, I call this development the "first stage of recovery." In rare instances no further progress occurs.

In a variable period of time (days, weeks or months), a return of reflex activity becomes evident with cystometric study. This activity is demonstrated by a gradually rising intravesical pressure as the bladder is filled and by minor reflex contractions believed to be due to the nerve mechanism within the baldder wall. These reflex contractions are inadequate, however, to empty the bladder of its contents. The term "autonomous cord bladder" is applied to this phase which has been called the "second stage of recovery."

Obviously, further recovery to the third or final stage is greatly to be desired and will be manifested in various ways depending upon the level of the injury and its extent. If attainment of the third stage prevails, several subdivisions must therefore be considered.

First, the patient with complete transection of the cervical or thoracic segments down to the level of T11 should eventually develop and show efficient reflex bladder contractions which are presumed to be activated by a reflex arc from the bladder to the spinal cord below the level of the injury. A sustained reflex contraction of at least 70 cm. of water is required for periodic efficient voiding, usually at capacities of 150–400 cc of urine. The term "automatic reflex bladder" has been used for this type of vesical activity.

Second, the patient with complete transection at the level of T12–L5, sometimes referred to as conus lesions, may or may not develop reasonably efficient reflex contractions of the bladder, but often emptying of the bladder can be facilitated only by manual pressure on the lower abdomen at the time of reflex contraction.

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Injuries incurred in civilian life might well be viewed in a different light from injuries sustained in war. In civilian life there is easy and rapid transportation to facilities for definitive treatment. At this time I prefer to discuss methods for care of civilian patients. Medical opinion concerning war casualties is a matter of record.

There is little doubt that two procedures of handling the bladder have become obsolete; namely, the Crede method without a catheter and intermittent catheterization.

The problem resolves itself either in the choice of an indwelling catheter connected to a closed system of drainage and irrigation with manual or automatic control (the latter known as tidal drainage), or suprapubic cystotomy with a closed system of drainage and irrigation, manual control. I believe that the bladder can recover to an optimum state by any of the three choices just mentioned. Naturally it will take longer when cystotomy is employed because of the lapse of time during closure of the suprapubic opening. When an adequate urethra, sterile apparatus and efficient personnel are available there would appear to be no reason to consider a cystotomy in civilian practice. I hold no preference for automatic over manual control of irrigation when either apparatus is available in perfect working condition. However, the assumption that urinary or genital complications never occur under the circumstances just described is, of course, false.

How long does it take for the bladder to recover after spinal cord injury? There are many variables to this question, such as level and extent of injury, presence or absence of infection, method of treatment, etc. In a relatively small series, Prather found that of the patients with complete transection, 62 per cent developed an automatic type of reflex voiding in an average of 6 months from the time of injury; while of those with partial transection, volunatry voiding was resumed in 98 per cent in approximately 3 months.

In a much larger series of 339 patients with a longer follow-up period, Bors reported eventual recovery in 91 per cent of lesions above the conus and in 97 per cent below the conus. Recovery occurred in 73–80 per cent within 10 months. He stated that restoration of function was about equally distributed between cases with complete and incomplete transection.

One should not deduce from the preceding remarks that the achievement of a satisfactorily working bladder in the paraplegic patient is simple. If this restoration were always effected easily, there would be no need for discussion of resection of the bladder neck, drugs for stimulation or relaxation of the bladder wall, nerve blocks to reduce bladder tone, or nerve blocks to relax the region of the external sphincter.

There are some patients whose bladders do not empty efficiently or whose capacity remains too limited for happy social existence. The following report of the work of others is related to show the methods of study and practice to overcome difficulties. They may be grouped into three plans of attack: 1) mechanical correction of bladder neck or urethral obstruction; 2) nerve blocks or resection to avoid imbalanced action by various nerve groups; 3) drugs to stimulate or repress nerve impulse.

In the presence of effective detrusor action as determined by cystometric study, some patients are unable to void, or, if able to void, leave a significant quantity of residual urine. This inability to empty the bladder would indicate an obstructive lesion at the bladder neck or in the region of the external sphincter mechanism. Griffiths demonstrated in dogs that urethral resistance was the same in the living and the dead and that it remained the same after division of the pudic nerve or after resection of the lumbar portion of the spinal cord. Likewise, Langworthy, Drew and Vest found that in the cat the collapsed urethra offered a resistance to the escape of urine which was not affected by resection of pudendal nerves, sacral roots or sympathetic fibres. Prather and Petroff made a urethrographic study of paraplegic patients and stated that dilatation of the bladder neck was a common finding in both the hypertonic and atonic type of bladder. In most instances, however, the region of the external sphincter was narrow as seen in the normal patient. Even though the urethrographic or cystoscopic findings were not typical of bladder neck obstruction in all cases, Emmett, Bumpus, Nourse and Thompson have freely advocated resection of this region and have reported excellent results. Multiple resections are said to be necessary at times. One always has to consider the relative balance between the power of the bladder wall and the obstructive potential of the bladder neck and urethral areas. A consideration of these factors accounts no doubt for the success of the procedure in some cases, as well as the failure in others. I personally dislike doing battle with the Don Quixote type of windmill that I cannot see. Talbot has stated that whenever there is persistent residual urine associated with what appears to be sufficient detrusor force as demonstrated cystometrically, resection is justified. Perhaps a fair evaluation of transurethral resection in the paraplegic patient has been stated by Bors whose extended experience in the Veterans Administration leads him to report that this operation will probably be indicated in five per cent or less of patients.

Concerning neurological procedures to facilitate proper bladder function, such as operations on nerves, I must quote others. From the known physiology of the bladder it does not seem probable that presacral neurectomy to interrupt sympathetic fibres offers hope of either stimulation or relaxation of the bladder wall, or that it changes resistance at the bladder neck. Pudendal nerve block or section has been mentioned by Sheldon and Bors in 26 patients with permanent improvement in 46 per cent, an accomplishment which deserves further evaluation. The aim, of course, is to diminish urethral resistance of the striated muscles of the perineum, particularly the external sphincter. Test with novocain block to observe the effect prior to a permanent procedure would appear desirable.

Sacral nerve blocks to diminish detrusor tone of the small capacity bladder have been reported, but I know of no large series for evaluation. Here again, novocain block, unilateral or bilateral, to observe the effects of the technique is desirable. If this method is effective in producing a bladder of larger capacity without destroying reflex activity, it should be worthwhile in the small capacity automatic reflex type of bladder. This approach deserves consideration from a theoretical point of view.

Drugs do not yet appear to have significant practical action on the paraplegic bladder either by stimulating reflex detrusor action or by causing relaxation of hypertonic muscle. However, Ney described a sufficient result from "furmethide" to cause vesico-ureteral reflux and induce a febrile pyelonephritis.

Thus it becomes evident that there are still problems for study. How can the bladder which has some unusual damage to its nerve supply be restored to a satisfactorily functioning organ. I refer, of course, to one which does not follow the normal path of recovery.

Perhaps more intensive study and refinement along the lines of sphincterometry, as developed by Simons and Rose and used by Bors would be helpful. In order to test various segments of the urethra for tissue resistance, the study might be made in conjunction with x-ray films to locate exactly the region tested. No doubt a large series of voiding cysto-urethrograms or observations of voiding during fluoroscopy would reveal valuable information. I know of no clinical efforts to induce bladder contractions in patients by electrical stimulation. Boundless gratitude is in store for those who may contribute to the solution of these problems.

Many patients with spinal cord injury are interested in the condition of the sexual mechanism as well as a properly functioning bladder. Prior to the recent war, data on sexual function in relation to spinal cord injury were practically nonexistent. During the war, attention was devoted to the salvage of the individual and his urinary tract. At present it is perhaps feasible to accumulate data of the sexual status and I summarize for you the studies may by Doctors Talbot, Horne, Paull and Munro at the Cushing Veterans Hospital near Boston. To my knowledge this work represents the first intensive study of this subject; it should serve as a stimulus to those who may be in a position to assemble further data.

Based on studies of 84 paraplegic patients, Horne, Paull and Munro report as follows: Erection takes place on a purely segmental reflex basis. Suprasegmental connections are unnecessary. In paraplegic patients the afferent sensory impulses that initiate the reflex are caused by tactile stimulation of the glans. The impulses then travel to the second, third and fourth sacral segments by way of the internal pudic nerve. Efferent impulses leave the same segments by way of the parasympathetic supply and cause dilation of the arterioles of the penis, with distention of the corpora cavernosa and spongiosum. In addition, efferent impulses leave the same segments over the internal pudic nerves to cause contraction of the periurethral muscles with resultant compression of venous drainage channels of the penis.

The studies of Horne, Paull and Munro indicate that destruction of the sacral segment of the cord or transection and destruction of the cauda equina and the pelvic parasympathetic plexuses are the only neurologic anatomic lesions that will prevent the occurrence of erections. Associated with the genital condition will be an autonomous bladder, an absent anal reflex and possibly atonic u sphincters. Erections may occur in the presence of all other cord injuries whe partial or complete, regardless of the level involved.

The studies of Horne, Paull and Munro also indicate that ejaculation is basically a complex purely segmental reflex function. Suprasegmental connections are not necessary for the act. Their evidence shows that ejaculation will be prevented by a destructive lesion of the sacral segments of the cord or a transecting lesion of the cauda equina. If damage is extensive enough and properly located in the spinal cord, ejaculation will also be prevented by either a transecting or partial injury between the sixth thoracic and third lumbar segments, depending on the degree of destruction of the sympathetic components in this area of the cord.

Talbot, during a study of 190 patients, noted that restoration of sexual function occurred as spinal shock disappeared, provided the reflex arc was intact. Of 105 patients with the level of injury at T11 or higher, 75 per cent retained the erectile reflex. Of 77 patients with lesions at lower levels, Talbot found that 50 per cent showed erections.

Fertility studies were also made by Horne, Paull and Munro on 18 patients. They obtained samples of semen with electrical stimulation by means of an active electrode through the rectum to the region of the seminal vesicles and prostate. This procedure was followed by massage of the organs and stripping of the urethra. They concluded that spinal cord injury in itself does not preclude fertility.

As demonstrated by the efforts of many, progress has been made and is still being made in the urological problems of spinal cord injuries. Continued effort and studies are needed in this fascinating field of physiology which is filled with the possibility of practical benefit to that most important individual—the patient.

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REFERENCES

Bors, E.: TB 10-53. Veterans Administration technical Bulletin Washington, D. C., Dec. 15, 1948.

Bors, E.: A simple cystometer. J. Urol., **60:** 287, 1948.

Bors, E.: Nerve Blocks. Conference on Care of Paraplegics. Washington, D. C., Jan. 15, 1948.

Bumpus, H. C., Nourse, M. H. and Thompson, G. J.: Treatment of the paraplegic. J. Urol., **57:** 1085, 1947.

Emmett, J. L.: Further observations in the management of cord bladder by transurethral resection. J. Urol., **57:** 29, 1947.

Griffiths, J.: Observations on the urinary bladder and urethra. J. Anat. and Physiol., **25:** 61, 1895.

Griffiths, J.: Observations on the urinary bladder and urethra. J. Anat. and Physiol., **25:** 254, 1895.

Heimburger, R. F., Freeman, L. W. and Wilde, N. J.: Sacral nerve innervations of the human bladder. J. Neurosurg., **5:** 154, 1948.

Horne, H. W., Paull, D. P. and Munro, D.: Fertility studies in the human male with traumatic injuries of the spinal cord and cauda equina. N. Eng. J. Med., **239:** 959, 1948.

Langworthy, O. R., Drew, J. E. and Vest, S. R.: Urethral resistance in relation to vesical activity. J. Urol., **43:** 123, 1940.

Martin, J. and Davis, L. Studies upon spinal cord injuries. Ann. Surg., **126:** 472, 1947.

Munro, D., Horne, H. W. and Paull, D. P.: The effect of injury to the spinal cord and cauda equina on the sexual potency of men. N. Eng. J. Med., **239:** 903, 1948.

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PATHOLOGICAL CHANGES IN URETHRA OF PARAPLEGIC PATIENTS

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From the Paraplegic Service of the Veterans Administration Hospital, Long Beach, California and the Department of Surgery, University of California at Los Angeles School of Medicine, Los Angeles, Calif.

This report deals with 43 cases of penoscrotal urinary fistula, 80 cases of penoscrotal urethral diverticulum and 7 cases of prostatic diverticulum, lesions infrequently encountered in nonparaplegic patients.

REVIEW OF LITERATURE

Etiology and classification. A decubitus ulcer forms in the urethra at the acute angle of the penoscrotal junction and subsequently develops into a peri-urethral abscess. A 22F Foley bag catheter was believed to cause peri-urethral abscess; however, fistulas were observed to develop even without the use of intra-urethral catheters. Trauma and infection may be the cause of such fistulas in nonparaplegic patients.

Urethral diverticula are either congenital or acquired. Congenital diverticula occupy the posterior, and acquired diverticula the anterior urethra. Congenital diverticula may be due to faulty closure of the urethral folds, hypoplasia of the corpus spongiosum or epithelial rests. An acquired diverticulum was observed in an older nonparaplegic man by external pressure of a glass urinal. Trauma, calculus, stricture, inflammation, cyst and perforation are generally accepted as causes for acquired urethral diverticula.

Another classification distinguishes between true and false diverticula. This latter classification, based upon the aneurysmatic nomenclature, is considered to be fallacious. Another detailed classification involves consideration of the congenital or acquired origin, the localization and the cause.

INCIDENCE AND DISTRIBUTION

Among 619 paraplegic patients 43 (6.9 per cent) had a penoscrotal fistula and 19 of these cases had associated diverticula. It was deemed desirable to screen at random paraplegics to determine what percentage of patients had diverticula. For this reason urethrograms were done on 122 patients, of which 61 (50 per cent) had diverticula. Only 7 (1.1 per cent) prostatic diverticula were encountered in the entire group of 619 patients.

The age of the 43 patients with fistulas and/or diverticula ranged from 19 to 56 years. The level of injury to the spinal cord was cervical in 10 cases, thoracic in 24 cases and lumbosacral in 9 cases. The lesion was considered clinically complete in 23 patients and incomplete in 20 patients. The time interval between injury and first observation of urethral pathology ranged from 1 month to 6 years.

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Of the 80 patients with diverticula at the penoscrotal junction, the level of the spinal cord lesion was cervical in 12 cases, thoracic in 58 cases and lumbosacral in 10 cases. The lesion was clinically complete in 53 patients and incomplete in 27 patients. The time interval between injury and first observation of urethral changes ranged from one month to thirteen years.

The ages of the 7 patients with a prostatic diverticulum ranged from 23 to 48 years. All patients had a complete lesion of the thoracic spinal cord. The time interval between injury and first observation ranged from 1 to 4 years.

All patients had worn catheters at some time, the caliber of which ranged from 16 to 18F. Some of the patients developed either a diverticulum or a fistula many months after the removal of the catheter.

SYMPTOMS AND DIAGNOSIS

The symptomatology of peri-urethral abscess, fistula or diverticulum differs in paraplegic and nonparaplegic patients in that all subjective manifestations related to micturition or pain are missing and only fever is present. Objective signs develop rapidly. Extension of a peri-urethral abscess to the scrotum may simulate epididymitis. Scrotal phlegmon has been observed.

Seepage of urine during micturition indicates a penoscrotal fistula. A diverticulum of the penoscrotal junction appears as a fluctuant mass and remains unnoticed before it attains considerable size because of the absence of subjective symptoms such as difficulty of micturition, terminal incontinence, decreased propulsive power or increased duration of micturition.

Prostatic diverticula may pose difficulties in establishing automatic micturition and are diagnosed by urethroscopy and urethrography. A 10 per cent skiodan solution is used for urethrography, with the patient lying on his back, and his penis held in a transverse position.

Penoscrotal diverticula were graded according to their respective diameter: grade 1, up to 1 cm.; grade 2, up to 2 cm.; grade 3, up to 3 cm.; and grade 4, up to and over 4 cm. Among 165 urethrograms, 58 (35.1 per cent) were grade 1, 14 (8.4 per cent) grade 2, 5 (3.0 per cent) grade 3, and 3 (1.8 per cent) grade 4.

MANAGEMENT

The management of penoscrotal fistulas or diverticula is threefold: a) conservative, b) conservative surgical, c) radical surgical.

Conservative management: Anemia, hypoproteinemia and infection must be corrected by transfusions, diet, sulfa drugs and antibiotics. Upper urinary tract disease must be eliminated. A 16F Foley bag catheter is taped to the abdomen of the patient (A. E. C.) in order to straighten and to splint the penoscrotal angle. The catheter is changed every 2 days with penicillin K.Y. jelly as a lubricant. Munro's training is used for cases with restored bladder function.

Conservative surgical management. A peri-urethral abscess is incised and drained. A fistula is treated by external or internal electrofulguration after 6 weeks. This can be repeated twice at 2 week intervals.

Radical surgical management. When the first two procedures fail, excision and repair are done. The method is the same for either urethral fistulas or diverticula at the penoscrotal junction. Two methods are applied (E. B.). The first consists of complete excision of the lesion from a transverse skin incision followed by transverse closure, with imbrication of extra-urethral flaps using fine atraumatic 0000 catgut sutures for all layers including the skin. The second method consists of complete excision of the fistula from a longitudinal incision with closure in three layers: A No. 32 stainless steel wire, introduced about 3 cm. below the inferior angle of the skin incision is used as a continuous extra mucosal inverting suture. The wire is brought out approximately 3 cm. superior to the upper angle of the skin incision and its ends are secured by buckshot according to Bunnell's technique of tendon sutures. A mattress wire suture No. 32 obliterates the dead space and is tied over small gauze pads. Three to five interrupted wire sutures, No. 32, are used for skin closure. Drainage is unnecessary. Hemorrhage is controlled by electrofulguration. A 16 Foley catheter attached to the abdominal skin, used as a splint, is changed after 7 days. Thereafter the catheter is changed biweekly for a period of 6 weeks. The skin sutures are removed on the seventh day, the mattress suture on the fourteenth day and the continuous extramucosal suture on the twenty-first day. A urethrogram is taken on the twenty-eighth day. Diversion of the urinary stream was practiced when severe infection was combined with a large diverticulum or when three attempts at closure failed. Smaller (grades 1 and 2) diverticula of the penoscrotal junction were not removed, provided that no back pressure could be demonstrated.

MANAGEMENT OF PROSTATIC DIVERTICULA

Diverticula extending below the posterior lip of the vesical neck are treated by incision of the lip (with the electrocautery) in order to establish wide communication with the urethra.

RESULTS

Table 1 presents the results of treatment of 40 cases with fistulas. Three patients remained untreated. Spontaneous healing occurred in 14 cases, in 2 without local treatment, in 12 despite treatment, but associated with the improvement of the patients' general health. Simple incision of the abscess cured 3 patients. Radical surgery yielded good results in 14 patients with the catgut technique and in 9 with wire technique. The urinary stream was diverted in 4 cases of the "catgut group" and in 5 patients of the "wire group" by suprapubic cystostomies or perineal urethrostomies. In the 10 cases of the "catgut group" in which diversion of the urinary stream was not done, 8 healed with one intervention while 2 required repeated operations. The remaining 4 cases with diversion required only one closure. Of the 9 patients treated with the wire technique, 4 responded to one closure without diversion. Among the remaining 5 treated with diversion. perineal urethrostomy was performed on 2 and 3 were admitted to this hospital with cystostomies.

Table 2 demonstrates the results of treatment of penoscrotal diverticula. Four cases were treated with the catgut technique and 6 with the wire technique.

Of the 80 patients with diverticula at the penoscrotal junction, the level of the spinal cord lesion was cervical in 12 cases, thoracic in 58 cases and lumbosacral in 10 cases. The lesion was clinically complete in 53 patients and incomplete in 27 patients. The time interval between injury and first observation of urethral changes ranged from one month to thirteen years.

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Radical surgical management. When the first two procedures fail, excision and

Incision of the neck of the diverticulum with the electrocautery was indicated and successful in 3 of the 7 patients with prostatic diverticula.

REPORTS OF HISTOLOGIC EXAMINATIONS

All diverticula of the anterior urethra were lined with stratified squamous epithelium with occasional transitional cells interposed. The fistulas were partly lined with stratified squamous epithelium, chiefly present at the urethral end, and were elsewhere lined by fibrous connective tissue which revealed inflammatory reaction.

DISCUSSION

The etiology of diverticula of the prostatic urethra in paraplegics is somewhat obscure, although one must assume that this condition is acquired. There appears to be a predisposing weakness, however, at the point of union between allantois, wolffian structures and cloaca which yields to pressure with the advent of infection and vesical dysfunction. The lack of reinforcement of the posterior part of the vesical neck by longitudinal muscle fibers and the frequently seen elevation of the posterior lip with trigonal retraction caused by dysfunction of the neurogenic bladder adds anatomico-physiological factors to the embryological considerations.

Penoscrotal fistulas and diverticula are acquired. The etiological similarity to decubitus ulcer is striking. The acute angulation at the penoscrotal junction is exposed to pressure. It may be a weak spot also as the site of the union of urethral and labial folds during the embryological development of the cavernous urethra and the scrotum. Pressure, internal by catheter or instrumentation or external by urinals may cause an ulcer.

The general condition of the patient is of importance for the development of any decubitus ulcer. Spontaneous cure of penoscrotal fistulas has been observed in 35 per cent of the patients in our series. Small fistulas have been treated by fulguration and large tracts by plastic methods. No unanimity of opinion exists concerning the necessity for diversion of the urinary stream in surgical repair. Some authors prefer suprapubic cystostomy to perineal urethrostomy. Cystostomy also was used when a transvesical de-roofing operation of a prostatic diverticulum was done. A two stage operation with diversion was proposed by others. Perineal urethrostomy alone cured some cases of penoscrotal fistulas. Successful closure of fistulas or diverticula at the penoscrotal angle without diversion was also reported. In our series, 9 cases of fistulas healed after the first intervention without diversion. Among 14 patients cured without diversion, 4 required two operations. Of the 10 patients with penoscrotal diverticulum only one, treated with diversion, failed to heal because of his lack of cooperation. The remaining 9 were cured without diversion, but 3 required two operations. No extensive plastic measures were done nor was the continuity of the urethra completely severed. Good mobilization is essential. The merits of stainless steel wire as suture material are known. Our extramucosal continuous wire suture served for the actual closure of the urethra and not to relieve only tension. The wire

There were 2 good results and 2 failures in the "catgut" group. One of these failures occurred despite diversion of the urinary stream. Among the 6 patients of the "wire" group, 5 required only one operation while one needed a second closure.

TABLE 1. *Treated fistulas* 40

Cure by:					
Spontaneous healing				*14*	(35%)
With unsuccessful preceding intervention		12			
Incision and drainage	6				
Incision and drainage (1 or more catgut closures)	1				
1 or more unsuccessful catgut closures	1				
Electrofulguration	2				
1 or more electrofulguration and 1 or more catgut closures	2				
Without preceding intervention		2			
Conservative methods (incision and drainage or electrofulguration)				*3*	(7 5%)
With unsuccessful other preceding intervention.		2			
Incision and drainage (catgut closure)	1				
Electrofulguration (catgut closure)	1				
Without unsuccessful other intervention		1			
Electrofulguration	1				
Radical surgery with catgut technique				*14*	(35%)
Without diversion		10	(25 0%)		
Healed with one intervention	8				
Healed with repeated interventions	2				
With diversion		4	(10%)		
Suprapubic cystostomy	2				
Perineal urethrostomy	2				
Radical surgery with wire technique				*9*	(22 5%)
Without diversion		4	(10%)		
Previous catgut failures	2				
Without previous intervention	2				
With diversion		5			
(Perineal) previous catgut and wire failures	2				
(Suprapubic) without previous local interventions	3				
Untreated fistulas (deceased)				3	

TABLE 2. *Treated penoscrotal diverticula*

			10
Radical surgery with catgut technique			*4*
Without diversion		3	
Successful with one closure	*1*		
Successful with two closures	1		
Unsuccessful with two closures and fulguration	1		
With diversion		1	
Unsuccessful with one closure	1		
Radical surgery with wire technique			*6*
Without diversion		6	
Successful with one closure	5		
Successful with two closures	1		

Incision of the neck of the diverticulum with the electrocautery was indicated and successful in 3 of the 7 patients with prostatic diverticula.

REPORTS OF HISTOLOGIC EXAMINATIONS

All diverticula of the anterior urethra were lined with stratified squamous epithelium with occasional transitional cells interposed. The fistulas were partly lined with stratified squamous epithelium, chiefly present at the urethral end, and were elsewhere lined by fibrous connective tissue which revealed inflammatory reaction.

DISCUSSION

The etiology of diverticula of the prostatic urethra in paraplegics is somewhat obscure, although one must assume that this condition is acquired. There appears to be a predisposing weakness, however, at the point of union between allantois, wolffian structures and cloaca which yields to pressure with the advent of infection and vesical dysfunction. The lack of reinforcement of the posterior part of the vesical neck by longitudinal muscle fibers and the frequently seen elevation of the posterior lip with trigonal retraction caused by dysfunction of the neurogenic bladder adds anatomico-physiological factors to the embryological considerations.

Penoscrotal fistulas and diverticula are acquired. The etiological similarity to decubitus ulcer is striking. The acute angulation at the penoscrotal junction is exposed to pressure. It may be a weak spot also as the site of the union of urethral and labial folds during the embryological development of the cavernous urethra and the scrotum. Pressure, internal by catheter or instrumentation or external by urinals may cause an ulcer.

The general condition of the patient is of importance for the development of any decubitus ulcer. Spontaneous cure of penoscrotal fistulas has been observed in 35 per cent of the patients in our series. Small fistulas have been treated by fulguration and large tracts by plastic methods. No unanimity of opinion exists concerning the necessity for diversion of the urinary stream in surgical repair. Some authors prefer suprapubic cystostomy to perineal urethrostomy. Cystostomy also was used when a transvesical de-roofing operation of a prostatic diverticulum was done. A two stage operation with diversion was proposed by others. Perineal urethrostomy alone cured some cases of penoscrotal fistulas. Successful closure of fistulas or diverticula at the penoscrotal angle without diversion was also reported. In our series, 9 cases of fistulas healed after the first intervention without diversion. Among 14 patients cured without diversion, 4 required two operations. Of the 10 patients with penoscrotal diverticulum only one, treated with diversion, failed to heal because of his lack of cooperation. The remaining 9 were cured without diversion, but 3 required two operations. No extensive plastic measures were done nor was the continuity of the urethra completely severed. Good mobilization is essential. The merits of stainless steel wire as suture material are known. Our extramucosal continuous wire suture served for the actual closure of the urethra and not to relieve only tension. The wire technique seems superior to catgut, since no foreign body is left behind and drainage is unnecessary. Five of the 6 patients so treated responded to the first operation, while one required a second intervention.

The timing of the intervention depends upon the condition of the bladder. It is ill advised to operate before bladder function has returned. An intra-urethral catheter, used for splinting and draining purposes, does not interfere with a good result, but recurrences appear with reintroduction of a catheter because of poor bladder function. Then perineal urethrostomy prior to closure is preferable until bladder function returns.

CONCLUSIONS

The following management of fistulas was considered practical: Peri-urethral abscesses should be incised and drained. An attempt at fulguration of the sinus tract is justified. If this fails, radical surgery with wire repair without diversion of the urinary stream may be attempted. In case of failure, diversion by perineal urethrostomy is preferred to suprapubic cystostomy, because it is believed that the urethrostomy interferes less with restored bladder function.

Urethral diverticula at the penoscrotal junction of grade 1 and grade 2 should be observed for back pressure. Diverticula of grade 3 and grade 4 require radical surgery.

A diverticulum of the prostatic urethra is best managed by transurethral incision of the neck of the diverticulum.

SUMMARY

Forty-three cases of penoscrotal urethral fistulas were found among 619 paraplegic patients. Nineteen had an associated diverticulum at the same location. An additional 61 cases with penoscrotal diverticulum and without fistula were found among 122 patients screened at random by urethrograms. Seven cases of prostatic diverticulum were observed.

The literature with special consideration of etiology and classification is reviewed.

The diagnosis is based upon routine cysto-urethroscopy and urethrography.

The conservative management attempts to improve the general health of the patient, conservative surgery uses incision of abscesses, fulguration of sinus tracts and electrofulguration of the roof of prostatic diverticula. Radical surgery resects either lesion at the penoscrotal junction.

Spontaneous healing of penoscrotal fistulas occurred in 35 per cent, conservative surgery succeeded in 7.5 per cent and radical surgery cured 57.5 per cent of the 40 treated cases. Three cases remained untreated.

Ten cases of large penoscrotal diverticula were healed by resection; 3 of the 7 cases with prostatic diverticula responded favorably to electric incision of the roof, 4 remained untreated.

Two methods were used for radical surgery consisting of a conventional catgut technique and a technique using wire exclusively. The latter was preferred. Diversion of the urinary stream was not used routinely.

The etiology, classification and results of treatment are discussed. An outline of management is offered in the conclusions.

REFERENCES

Attwater, H. L. and Hughes, J. R.: Repair of a fistula of the penile urethra. Lancet, **235**: 569, 1938.

Bell, J. G. Y.: Tuberculosis of the epididymis: Four cases of urinary fistula following orchidectomy. Brit. J. Urol., **5**: 114–124, 1937.

Bors, E.: Spinal cord injuries. Veterans Administration Technical Bull. TB10-503, December 15, 1948.

Bors, E. and Comarr, A. E.: Ischial decubitus ulcer. Surgery, **24**: 680, 1948.

Bunnell, S.: Surgery of the Hand. Philadelphia: J. B. Lippincott Co., 1944.

Cabanie, G.: Uretrectomie parcellaire pour fistules uretrales. Conditions d' execution et details de technique. J. d' urol., **52**: 66, 1944.

Comarr, A. E.: Management of decubitus ulcers in paraplegia. Ann. West. Med. & Surg., **3**: 235, 1949.

Cordonnier, J. J.: Fistula of the penile urethra. J. Urol., **55**: 278, 1946.

Derra, E. and Nadermann, E.: Parossale Verkalkungen an den Beinen bei Paraplegikern Nach Wirbelbruchen. Zentralbl. f. Chir., **69**: 758, 1942.

Emmett, J. L., Daut, R. V. and Dunn, J. H.: Role of the external urethral sphincter in the normal bladder and cord bladder. J. Urol., **59**: 439, 1948.

Hayes, B. A.: Treatment of urethral fistula. J. Oklahoma State Med. Assoc., **31**: 33, 1938.

Huber, K. and Kyrle, P.: Ueber das Auftreten von Harnrohren fisteln bei Ruckenmarkschadigungen: Wiener klin. Woch. Schr., **55**: 426, 1942.

Johnson, F. P.: Diverticula and cysts of the urethra. J. Urol., **10**: 295, 1923.

Knox, W. G.: Congenital diverticulum of the male urethra. J. Urol., **58**: 344, 1947.

LeComte, R. M. and Herschman, M. J.: Diverticula of the male urethra. J. Urol., **30**: 463, 1933.

Lowsley, O. S. and Gutierrez, R.: Diverticulos de la urethra. Rev. de Med. Y Cirurg. Habana, April 1928.

Lowsley, O. S. and Kirwin, T. J.: Clinical Urology. Baltimore: Williams & Wilkins Co., 1944.

McCrea, E. D'A.: The musculature of the bladder. Proc. of Royal Soc. Med. J. (Sec. of Urology), **19**: 35, 1926.

McKay, R. W. and Colston, J. A. C.: Diverticula of the male urethra. Surg. Gynec. & Obst., **48**: 51, 1929.

Moucat, T. B.: Urethral diverticula. Brit. J. Surg., **16**: 51, 1928.

Munro, D.: The rehabilitation of patients totally paralyzed below the waist with special reference to making them ambulatory and capable of earning their living. III. Tidal drainage, cystometry and bladder training. New Eng. J. Med., **236**: 223, 1947.

Ostry, H.: Diverticulum of urethra in a male. Canada M.A.J., **58**: 68, 1948.

Petroff, B. P.: The paralyzed patient: Urologic aspects. J. A. M. A., **129**: 154, 1945.

Powell, N. B.: The use of alloy stainless steel wire in closing urological wounds. J. Urol., **56**: 35, 1946.

Prather, G. C.: Urological Aspects of Spinal Cord Injuries. Springfield, Ill.: Charles C Thomas, 1949.

Stone, E. P.: Functional evolution of the neurogenic bladder in paraplegic patients. J. Urol., **63**: 673, 1950.

Talbot, H. S.: Cystometry, and the treatment of vesical dysfunction in paraplegia. J. Urol., **59**: 1130, 1948.

Thompson, G., Nourse, M. H. and Bumpus, H. C.: Treatment of the paraplegic: Observation in a series of 101 cases. J. Urol., **57**: 1085, 1947.

Watts: Quoted by McKay and Colston.

Waugh, J. R.: Diverticula of the urethra caused by periurethral abscess. J. Urol., **28**: 619, 1932.

Wesson, M. B.: Anatomical, embryological, physiological studies of the trigone and neck of the bladder. J. Urol., **4**: 279, 1920.

Young, H. H. and Shaw, E. C.: Urethral diverticula. South. Med. J., **19**: 42, 1926.

Young, H. H. and Wesson, M. B.: The anatomy and surgery of the trigone. Arch. Surg., **3**: 1, 1921.

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Millin's operation is now enjoying a spectacular acceptance in England and elsewhere. This operation avoids many of the disadvantages inherent in perineal prostatectomy to the extent that some of the ardent advocates of the latter are going over to the retropubic technique. But some urologists have credited the safety of the Millin operation not so much to the novel anatomic approach as to the employment of modern surgical principles; for the operation was tried before and abandoned. The answer to this question must await the comparison of accumulated series of cases performed by all the techniques of prostatectomy in which modern surgical methods are employed.

Certainly the dangers of open prostatectomy have been reduced to a point where the mortality of these operations is approaching that of transurethral resection. Whether the open techniques of prostatectomy will ever attain the popularity among patients that endoscopic surgery enjoys is another question: and the personal opinion of partisan urologists cannot be depended upon for the answer.

Let us now consider one of the conditions in which poor results often follow transurethral resection. One often hears the remark that transurethral resection is ideally adapted to the treatment of vesical neck contracture and such lesions. True, the mechanics of removing the obstruction with a resectoscope in these cases are quite simple: most any neophyte can perform the operation. But getting a satisfactory result is often quite another matter. There are two distinct groups of cases in which difficulties arise, and they will be discussed separately.

First, is the patient who has a well defined contracture of the bladder neck with a large amount of residual urine. One rarely encounters a case of median bar or vesical neck contracture in which complete retention occurs. On the contrary, these patients often void a stream having a fairly good caliber. The bladder musculature in these cases decompensates gradually and when the urologist sees the patient he usually finds that the amount of residual urine is exceedingly large. Furthermore, a cystometric examination will disclose an absent or diminished sensation, with the result that the voiding reflex is altered or virtually abolished. Likewise, the bladder tonicity is low—so that the pressure curve made while filling the bladder to capacity is flat, like the curve of a tabetic bladder. This type of bladder is not rehabilitated simply by removal of the obstructive lesion, and the patient will continue to void urine ineffectively following resection no matter how well the operation has been performed. Acetylcholine and

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TRANSURETHRAL PROSTATIC RESECTION: A DISCUSSION OF SOME PRINCIPLES AND PROBLEMS

REED M. NESBIT

Eighteen years have elapsed since the resectoscope flashed like a comet across the urological skies, leaving in its wake a trail of sepsis, incontinence, strictures, ruptured bladders and heartaches; as well as partisan argumentation. But the operation has survived and its present accepted place has been established in spite of all of the adverse criticism of the pessimists and the cynics as well as the over-enthusiastic platitudes uttered by its staunchest advocates; for each group influenced the development of endoscopic prostatic surgery in the democractic way that characterizes genuine scientific progress.

I have been asked to discuss the subject of transurethral prostatic resection with you tonight, and since your program committee has not specified just what aspect of this subject should be dwelt upon your speaker will talk on several phases of the subject.

THE INDICATIONS FOR TRANSURETHRAL PROSTATIC RESECTION

One is often asked the question, "What are the indications for transurethral prostatic resection?" The answer invariably will depend upon who makes the reply. There are some well known urologists who would say, "Any case with an obstructive lesion at the bladder outlet." There are some at the other end of the spectrum who would reply, "only in bladder neck contractures, and infiltrating cancer of the prostate with obstruction." The rest of us mostly perform transurethral resection in any obstructed patient who has a prostate gland that we believe can be subtotally removed with a resectoscope in a reasonable period of operating time. Other cases are submitted to enucleative methods of prostatectomy.

What about suprapubic, retropubic and perineal prostatectomy? Twenty-five years ago the suprapubic operation carried a mortality rate of about 20 per cent in the best of hands. That fact made the low mortality of perineal prostatectomy a convincing selling point in spite of the recognized risks of incontinence, rectal fistulas and sexual impotence which then as now endangered the performance of the operation. But our surgical generation has witnessed revolutionary advances in methods which have increased the safety of all surgery and nowhere has the benefit of this change been more advantageously employed than in the surgery of the aged, especially the prostatic patient.

Today the mortality of suprapubic prostatectomy is nearly as low as that of the perineal operation. As a result many surgeons believe that the risks inherent in the perineal approach have been more than balanced in favor of the suprapubic operation. My own inclination in the matter is to agree with this viewpoint but it is quite evident that in certain cases perineal prostatectomy con-

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Read at meeting of Texas Urological Society, November 1949; the Urology Postgraduate Convention of the North Central Section, American Urological Association, December 5, 1949; and at the Postgraduate Urological Seminar, Mid-Atlantic Section, American Urological Association, Baltimore, Febraury 2, 1950.

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When the residual urine is not excessively large following resection, the patient may effectively reduce its amount at each urination by the use of supplementary extra-abdominal pressure during urination. But some patients, even after prolonged drainage will be found to empty the bladder ineffectively and some of these individuals will empty their bladders completely only after partial cystectomy in which the upper portion of the bladder, permanently atonic, is excised.

The other type of case which often yields unsatisfactory results after transurethral resection is the one in which the patient complains of frequent urination, moderate difficulty in voiding, and an absence of residual urine, or at most, a small amount. Cystoscopy reveals moderate vesical trabeculation and a minimal to moderate contracture of the vesical neck. Usually there is no infection present, but if present, its eradication fails to relieve the patient of his symptoms. The competent and conscientious urologist employs every available method to treat this patient yet the man continues to return with his complaint. Finally in desperation he performs a resection of the vesical outlet. If all resections in this type of case resulted in failure the problem would be a simple one: we would never operate on any of them; but many of the patients are completely and permanently relieved by resection. The remainder are the ones that are as a millstone about the neck of the surgeon who operates upon them; their symptoms are not relieved or some become worse. We all have had that regrettable experience. Some of the patients finally drift to another urologist, some end up in the office of an attorney, but neither alternative brings satisfaction to the unhappy patient.

How is one to avoid this type of situation—how differentiate the real from the spurious? The answer is not an easy one but experience has taught the desirability to exert extreme conservatism in dealing with these individuals, and when resection is resorted to, the urologist will be well advised to warn his patient that the operation may fail of its purpose. But even when forewarned, the patient who is unrelieved remains unhappy and disgruntled. This particular type of case brings to mind the experience that surgeons once had in treating duodenal ulcer by operation. Most of the procedures failed to provide lasting relief of symptoms to an extent that today the condition is treated almost exclusively by medical regimens, and only when this treatment fails is surgery resorted to: then radical excision of the pyloric end of the stomach is carried out. Perhaps urologists will some day arrive at a similar point of view regarding the treatment of the irritative prostate gland, and utilize operation only as a last resort; then perform total perineal prostatectomy. But the obvious advantage of this alternative would doubtless have dubious value when weighed against the certainty of complete sexual impotence; for most of the patients who suffer the disturbance in question are men in the fourth and fifth decades and have not yet lost their sexual desire.

NOTES ON THE TECHNIQUE OF OPERATION

Most urologists who use the loop resectoscope have learned that movement of the entire instrument while cutting will facilitate the excision of long pieces of tissue. Also they have found it advantageous to cut several fragments of tissue before removing the working element of the instrument. This speeds up the matter of getting along with the job at hand.

There are many techniques of attacking the benign gland and it is not the purpose of the present discussion to dwell upon the method that has been routinely employed in our clinic. This, and other techniques, have been described and literature is available for those who are interested in the matter. However, I will discuss a few points in technique which often bring inquiry from visiting neophyte resectionists.

Is perineal urethrotomy necessary and how often is it used?

Resectoscopes are now available in three sizes: 24, 26 and 28F. When the resectionist uses a convertible instrument having all three sizes he seldom encounters a patient who needs meatotomy and rarely finds the need for perineal urethrotomy because of limited urethral caliber. However, we believe that in cases where the suspensory ligament of the penis is so short as to make instrumentation difficult, perineal urethrotomy enhances safety in performing resection. The resectionist is well advised to follow this rule: Any time the resectoscope fails to glide freely in the urethra like a bow on a violin, damage will surely result. Perineal urethrotomy is easy to perform, and harmless, whereas instruments tightly held by the urethra are extremely dangerous.

Another aid in technique is the control of priapism. This occasionally develops when the resectoscope is introduced and complicates the technique of operation. Dr. Rigdon Ratliff of Ann Arbor recently found that administration of curare intravenously would result in a complete and prompt subsidence of this disturbance.

THE USE OF DIGITAL PALPATION BY RECTUM WHILE RESECTING TISSUE

Many urologists have found this maneuver to be an indispensable aid to the performance of subtotal endoscopic prostatectomy. There are many capable resectionists who do not utilize this guide and there should be no quarrel to make with surgeons who have developed successful techniques that exclude this important feature. But less experienced resectionists will do well to use palpation along with vision in performing resection. Why deprive themselves of the sense of touch in performing a delicate operation which at best is difficult to perform?

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One phase of operative technique that appears not to be widely understood is recognition of the external sphincter.

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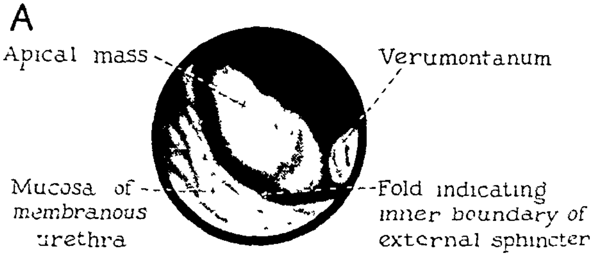
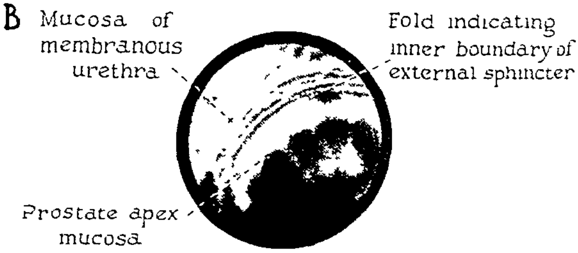
The beginning resectionist often encounters difficulty in deciding just where to stop in removing tissue at the apex of the prostate gland. If he removes too little at this site, the remaining tissue expands and bulges into the urethra and produces additional obstruction to urination. If he removes too much the external sphincter may be injured and the patient will become incontinent. However, it is necessary to remove all of the apical tissue with great precision if an excellent operative result is to be assured. Many authors have asserted that the verumontanum provides a reliable landmark to determine how far the resectionist should extend the cutting maneuvers, but experience has demonstrated that the position of the verumontanum often varies in its relationship to the distal border of the hypertrophied gland; so the verumontanum does not provide a determinative end point for cutting.


A
Apical mass
Verumontanum
Mucosa of membranous urethra
Fold indicating inner boundary of external sphincter

Apex viewed Posteriorly

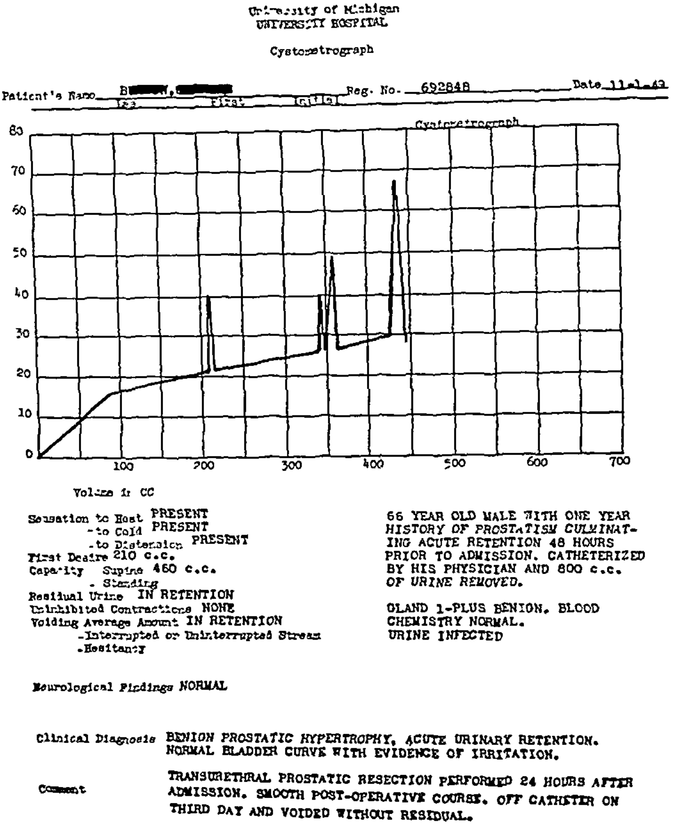

B
Mucosa of membranous urethra
Fold indicating inner boundary of external sphincter
Prostate apex mucosa

Apex Viewed Anteriorly to Localize External Sphincter

FIG. 1. Endoscopic view of junction between prostatic and membranous urethra in nodular hyperplasia. Fold which delineates this junction is accentuated by movement of tissues with resectoscope.

A simple and accurate method of delineating the exact end point for cutting is the one which the present author described in *New England Journal of Medicine* (August 1947). There is a visible point of junction between the prostatic urethra and the membranous urethra which depends for its delineation upon the fact that the membranous urethra is a fixed structure while the prostate gland is movable. The mucosa which bridges this junction forms a fold or wrinkle when the prostate is moved, like the wrinkling of the bellows that join two Pullman cars. This line (fig. 1), like the naso-labial fold on the human face, is present in all individuals; it is faintly discernible in some, deeply etched in others, yet can be accurately traced in all. It marks the outer limit for safe cutting. The resectionist can hew to this line by moving the instrument so that the line corresponds in position with the end of the fenestra, for one can cut only the tissues which are in the field of vision.

The apex tissue must be removed with meticulous care all the way to the external sphincter, but removal of only the tissues that project into the urethra in this area will fall short of adequate. The apical masses that abut upon the triangular ligament often extend for some distance laterally, and must be removed in their entirety. Lateral excavation that involves their removal is enhanced by the guidance afforded by counter pressure and digital palpation by a finger in the rectum.


University of Michigan
UNIVERSITY HOSPITAL

Cystometrograph

Patient's Name B[redacted], [redacted] Reg. No. 692848 Date 11-1-42
Last First Initial

Sensation to Heat PRESENT
-to Cold PRESENT
-to Distension PRESENT
First Desire 210 c.c.
Capacity Supine 460 c.c.
- Standing
Residual Urine IN RETENTION
Uninhibited Contractions NONE
Voiding Average Amount IN RETENTION
-Interrupted or Uninterrupted Stream
-Hesitancy

66 YEAR OLD MALE WITH ONE YEAR HISTORY OF PROSTATISM CULMINATING ACUTE RETENTION 48 HOURS PRIOR TO ADMISSION. CATHETERIZED BY HIS PHYSICIAN AND 800 c.c. OF URINE REMOVED.

GLAND 1-PLUS BENIGN. BLOOD CHEMISTRY NORMAL.
URINE INFECTED

Neurological Findings NORMAL

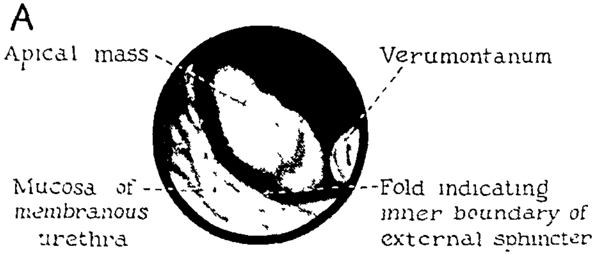
Clinical Diagnosis BENIGN PROSTATIC HYPERTROPHY, ACUTE URINARY RETENTION. NORMAL BLADDER CURVE WITH EVIDENCE OF IRRITATION.

Comment TRANSURETHRAL PROSTATIC RESECTION PERFORMED 24 HOURS AFTER ADMISSION. SMOOTH POST-OPERATIVE COURSE. OFF CATHETER ON THIRD DAY AND VOIDED WITHOUT RESIDUAL.

FIG. 2. Cystometric curve; well compensated bladder. Postprostatectomy micturitional function will be normal.

One other point regarding the performance of operation should be mentioned even at the risk of being repetitious. The risks of hemolysis entailed by the use of plain water as an irrigating medium have been adequately demonstrated since

The beginning resectionist often encounters difficulty in deciding just where to stop in removing tissue at the apex of the prostate gland. If he removes too little at this site, the remaining tissue expands and bulges into the urethra and produces additional obstruction to urination. If he removes too much the external sphincter may be injured and the patient will become incontinent. However, it is necessary to remove all of the apical tissue with great precision if an excellent operative result is to be assured. Many authors have asserted that the verumontanum provides a reliable landmark to determine how far the resectionist should extend the cutting maneuvers, but experience has demonstrated that the position of the verumontanum often varies in its relationship to the distal border of the hypertrophied gland; so the verumontanum does not provide a determinative end point for cutting.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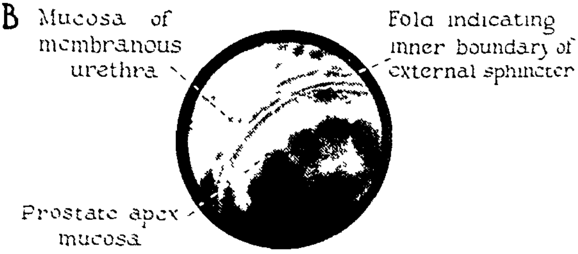
Apical mass
Verumontanum
Mucosa of membranous urethra
Fold indicating inner boundary of external sphincter

Apex viewed Posteriorly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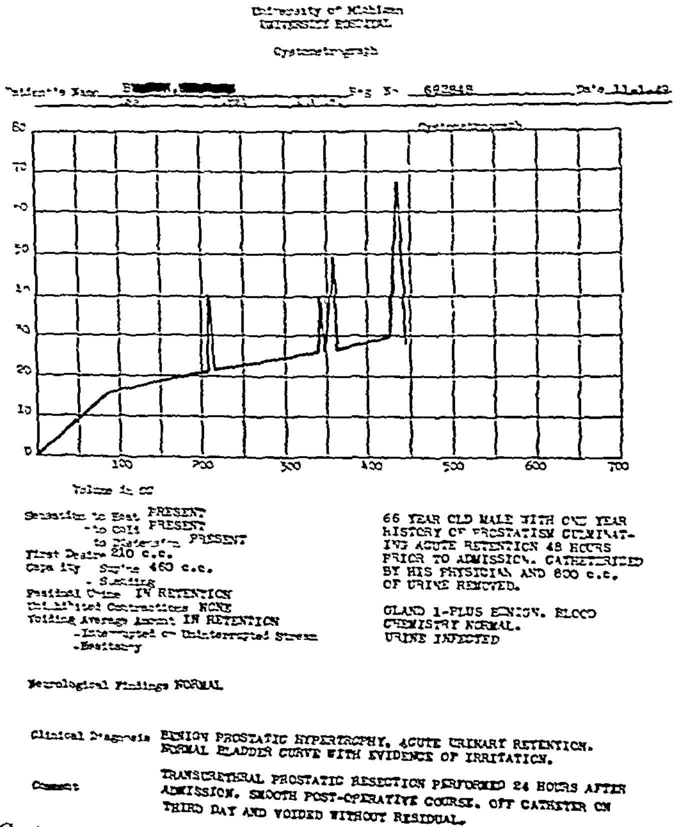

University of Michigan
UNIVERSITY HOSPITAL

Cystometrogram

Patient's Name [redacted] Reg No 692848 Date 11-1-42

Sensation to Heat PRESENT
-to Cold PRESENT
to Distension PRESENT
First Desire 210 c.c.
Capacity Supine 460 c.c.
- Standing
Residual Urine IN RETENTION
Uninhibited Contractions NONE
Voiding Average Amount IN RETENTION
-Interrupted or Uninterrupted Stream
-Hesitancy

66 YEAR OLD MALE WITH ONE YEAR HISTORY OF PROSTATISM CULMINATING ACUTE RETENTION 48 HOURS PRIOR TO ADMISSION. CATHETERIZED BY HIS PHYSICIAN AND 800 c.c. OF URINE REMOVED.

GLAND 1-PLUS BENIGN. BLOOD CHEMISTRY NORMAL.
URINE INFECTED

Neurological Findings NORMAL

Clinical Diagnosis BENIGN PROSTATIC HYPERTROPHY. ACUTE URINARY RETENTION. NORMAL BLADDER CURVE WITH EVIDENCE OF IRRITATION.

Comment TRANSURETHRAL PROSTATIC RESECTION PERFORMED 24 HOURS AFTER ADMISSION. SMOOTH POST-OPERATIVE COURSE. OFF CATHETER ON THIRD DAY AND VOIDED WITHOUT RESIDUAL.

FIG 2 Cystometric curve, well compensated bladder. Postprostatectomy micturitional function will be normal

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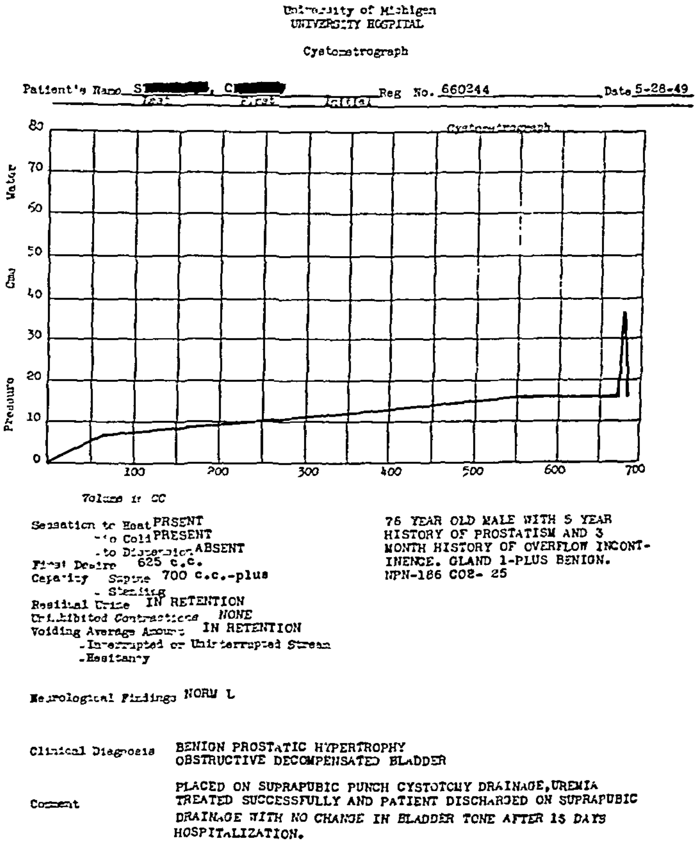
Creevy first reported this hazard of transurethral resection. Most urologists today acknowledge the advantage of using a *nonhemolizing solution for irrigation*, yet many resectionists continue to use plain water today, either because they find that it is too much bother or too expensive. Such an attitude is deplorable and is altogether too cynical for a modern urologist.

The operative mortality of all types of prostatectomy has been reduced to a point where the urologist is able successfully to perform one stage operations upon patients who a few years ago could not have been saved even with two stage operations. One result of this increase in the safety of operation has been that some urologists have been emboldened in the matter of performing endoscopic prostatectomy in patients having nitrogen retention. The argument in favor of this unusual practice is that early operation will provide natural drainage for the obstructed urinary tract and will at the same time avoid prolonged catheter drainage which of itself is hazardous. Whether this practice is to be deplored or condoned is a moot question. Some of our more venturesome urologists have reported success in following this course. My own opinion in the matter is that the average resectionist does not possess the technical skill to warrant the risks



University of Michigan
UNIVERSITY HOSPITAL

Cystometrograph

Patient's Name S[redacted], C[redacted] Reg No. 660244 Date 5-28-49
Last First Initial

Sensation to Heat PRSENT
-to Cold PRESENT
-to Distension ABSENT
First Desire 625 c.c.
Capacity Supine 700 c.c.-plus
- Standing
Residual Urine IN RETENTION
Uninhibited Contractions NONE
Voiding Average Amount IN RETENTION
-Interrupted or Uninterrupted Stream
-Hesitancy

76 YEAR OLD MALE WITH 5 YEAR HISTORY OF PROSTATISM AND 3 MONTH HISTORY OF OVERFLOW INCONTINENCE. GLAND 1-PLUS BENION. NPN-186 CO2- 25

Neurological Findings NORM L

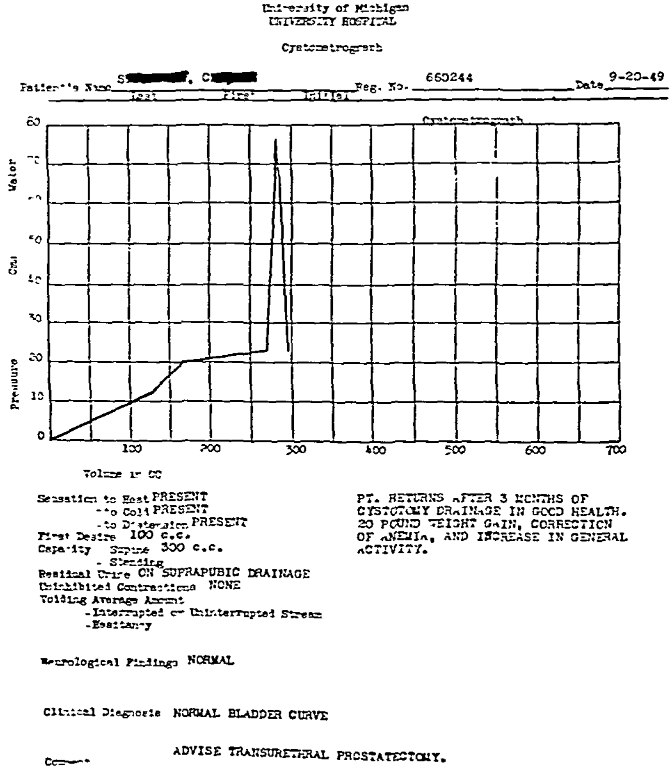
Clinical Diagnosis BENION PROSTATIC HYPERTROPHY
OBSTRUCTIVE DECOMPENSATED BLADDER

Comment PLACED ON SUPRAPUBIC PUNCH CYSTOTOMY DRAINAGE,UREMIA TREATED SUCCESSFULLY AND PATIENT DISCHARGED ON SUPRAPUBIC DRAINAGE WITH NO CHANGE IN BLADDER TONE AFTER 15 DAYS HOSPITALIZATION.

FIG. 3. *After catheter drainage for 15 days; bladder atonic.*

entailed in operating upon patients who are still uremic. If all goes well, and in the majority of his operations this can be expected, he will have no difficulty and his patients will benefit by the surgeon's boldness. But if any complications arise, as must occasionally be expected in most hands, the chances of survival are importantly jeopardized.

We urologists will do well to remind ourselves that the uremic state is always accompanied by serious dislocations in the chemical economy of the body and that prostatectomy, no matter how skillfully performed, possesses inherent risks that are greater than the risks of temporary catheter drainage or suprapubic puncture cystotomy drainage. Let us look with admiration upon the skill of the exceptional surgeons who can perform enucleative or endoscopic prostatectomy in these cases with success, but let us not try to compete with them; their virtuosity like that of the daring tight rope walker is more safely envied than emulated.


University of Michigan
UNIVERSITY HOSPITAL

Cystometrograph

Patient's Name S[redacted], C[redacted] Reg. No. 660244 Date 9-20-49
Last First Initial

Sensation to Heat PRESENT
-to Cold PRESENT
-to Distension PRESENT
First Desire 100 c.c.
Capacity Supine 300 c.c.
- Standing
Residual Urine ON SUPRAPUBIC DRAINAGE
Uninhibited Contractions NONE
Voiding Average Amount
-Interrupted or Uninterrupted Stream
-Hesitancy

PT. RETURNS AFTER 3 MONTHS OF CYSTOTOMY DRAINAGE IN GOOD HEALTH. 20 POUND WEIGHT GAIN, CORRECTION OF ANEMIA, AND INCREASE IN GENERAL ACTIVITY.

Neurological Findings NORMAL

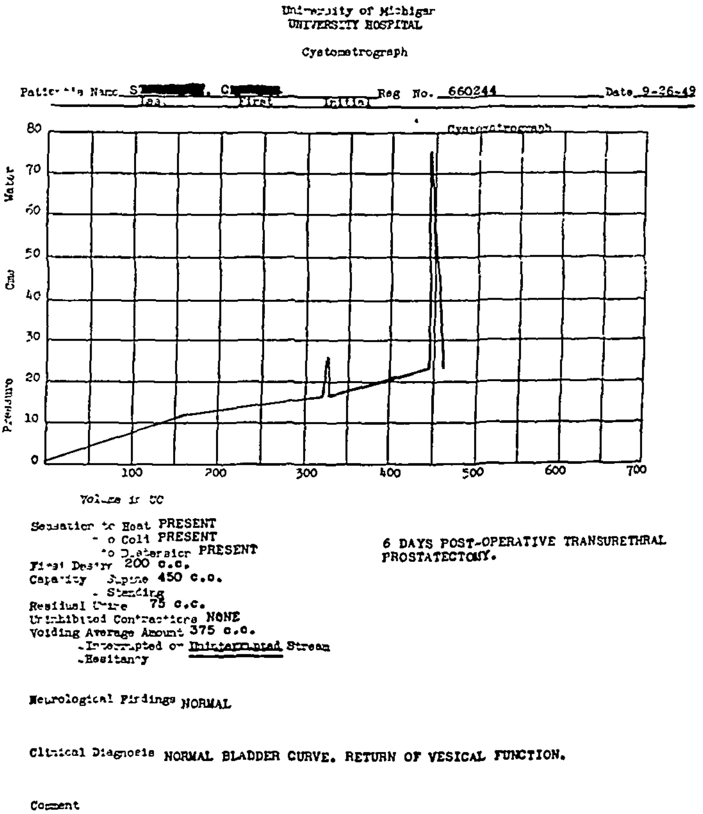
Clinical Diagnosis NORMAL BLADDER CURVE

Comment ADVISE TRANSURETHRAL PROSTATECTOMY.

FIG. 4. Same case as figure 3. Four months of suprapubic drainage have resulted in return of tonicity.

Another result of the increased safety of prostatic surgery, and in this instance more insidious than the practice just discussed, is operating upon a group of cases not uremic, that formerly were always placed upon prolonged drainage. These patients are characterized by a state of poor nutrition commonly associated with cardiac, pulmonary or cerebrovascular disease, or just old age. The bladder musculature too reflects the general debility and apparently has insufficient expulsive power to empty, in spite of complete removal of the prostate gland.

In those patients with decompensated bladders but who are otherwise in good general health it is common observation that with the removal of the prostate the bladder rapidly compensates along with subsequent improvement and well being. However, in those patients who are handicapped by serious and debilitating disease, or who are enfeebled by senescence, the decompensated bladder regains muscular strength slowly and the patient carries a high residual urine or requires urethral catheter drainage for a prolonged period. It is during this period of time that complicating infections, acute and chronic, carry the patient to his death.



University of Michigan
UNIVERSITY HOSPITAL

Cystometrograph

Patient's Name [redacted], [redacted] Reg No. 660244 Date 9-26-49
Last First Initial

Sensation to Heat PRESENT
- to Cold PRESENT
- to Distension PRESENT
First Desire 200 c.c.
Capacity Supine 450 c.c.
- Standing
Residual Urine 75 c.c.
Uninhibited Contractions NONE
Voiding Average Amount 375 c.c.
- Interrupted or Uninterrupted Stream
- Hesitancy

6 DAYS POST-OPERATIVE TRANSURETHRAL PROSTATECTOMY.

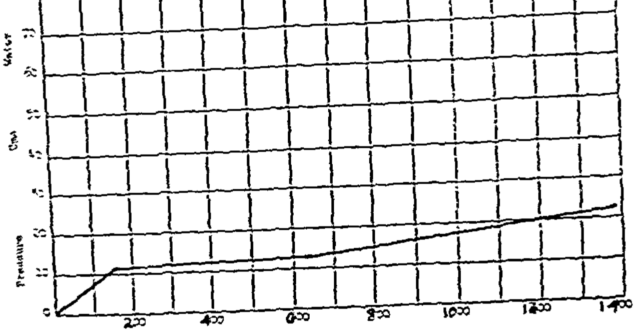
Neurological Findings NORMAL

Clinical Diagnosis NORMAL BLADDER CURVE. RETURN OF VESICAL FUNCTION.

Comment

FIG. 5. Same case as figure 3. Cystometric curve 6 days after prostatectomy; normal micturitional function.

In our hands this situation has accounted for about a third of the deaths that have occurred following transurethral resection during the past two years. In that period of time 675 patients had endoscopic prostatectomy in the University of Michigan Hospital and ten died in the hospital following operation, a mortality rate of 1.48 per cent. On critical analysis most of the deaths appear to have



Volume in CC

Sensation to Heat PRESENT
- to Cold PRESENT
- to Distension DIMINISHED
First Desire 400 c.c.
Capacity - Supine 1350 c.c.
- Standing
Residual Urine IN RETENTION
Uninhibited Contractions NONE
Voiding Average Amount IN RETENTION
- Interrupted or Uninterrupted Stream
- [illegible]

69 YEAR OLD MALE WITH TWO YEAR HISTORY OF PROSTATISM AND 3 WEEK HISTORY OF OVERFLOW INCONTINENCE.
BLOOD CHEMISTRY NORMAL.
GLAND 1-PLUS BENIGN

Neurological Findings NORMAL

Clinical Diagnosis BENIGN PROSTATIC HYPERTROPHY
OBSTRUCTIVE DECOMPENSATED BLADDER

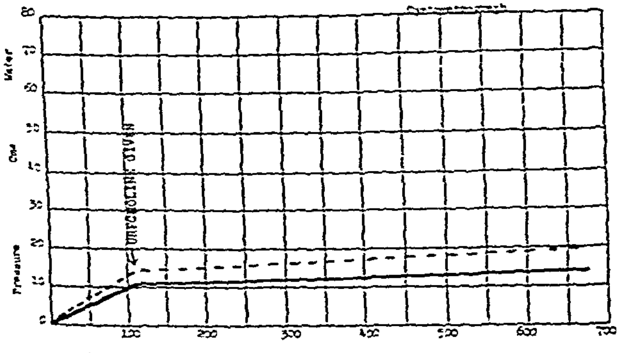
Comment PLACED ON SUPRAPUBIC PUNCH CYSTOTOMY. CYSTOMETRIC CURVE ONE WEEK AFTER CYSTOTOMY IDENTICAL TO THAT ABOVE.
DISCHARGED ON CYSTOTOMY.

FIG. 6. Cystometric curve on admission: atonic patient placed on suprapubic drainage.

University of Michigan
UNIVERSITY HOSPITAL

Cystometrograph

Patient's Name [redacted] Reg. No. 511110 Date 9-28-49
Last First Middle



Volume in CC

Sensation to Heat PRESENT
- to Cold PRESENT
- to Distension PRESENT
First Desire 450 c.c.
Capacity - Supine 670 c.c.
- Standing
Residual Urine 395 c.c.
Uninhibited Contractions NONE
Voiding Average Amount 100 c.c.
- Interrupted or Uninterrupted Stream
- [illegible]

Neurological Findings NORMAL

Clinical Diagnosis CYSTOMETRIC 6 DAYS POST-OPERATIVE TRANSURETHRAL PROSTATECTOMY
VOIDS WITH 395 c.c. RESIDUAL. POOR DETRUSOR TONE
TRIAL OF URECHOLIN SHOWS NO RESPONSE

Comment REPEAT EXAMINATION AFTER TEN DAYS ESSENTIAL THE SAME
DISCHARGED ON FURTHER SUPRAPUBIC DRAINAGE.

FIG. 7. Same case as figure 6. After 4 months of drainage, curve still that of atonic bladder. Following prostatectomy patient was able to urinate satisfactorily by straining, but had large amount of residual urine. Continued suprapubic drainage is indicated until normal tonicity retur[illegible] fails, then partial cystectomy might eventually be indicated.

been unavoidable but three of the cases fell into the group under present discussion. In retrospect one must conclude that these deaths might have been avoided by restricting our indications for transurethral resection and enlarging our utilization of preliminary puncture cystotomy drainage. To be sure, the safety of transurethral resection in these cases has been adequately demonstrated, for they survived the operation; but they finally went on to die from the complications of adynamic bladder dysfunction which we improperly treated. Prompt drainage, not early prostatectomy was indicated.

In an attempt to distinguish which cases fall into this group we now make it a practice to put all such patients on urethral catheter drainage temporarily and observe the bladder tone by cystometry. The cystometric curve in a well compensated bladder that is on catheter drainage demonstrates a normal curve or a shift to the left of normal (fig. 2). The curve of a bladder suffering from adynamic muscular dysfunction is flat like the curve seen in tabes dorsalis. Some adynamic bladders will compensate after a few days of catheter drainage and in these the cystometric curve will show a shift to normal or to the left of normal. (figs. 3, 4 and 5). Such patients will probably have good micturitional function after prostatectomy. But if the bladder remains adynamic after several days of catheter drainage, prostatectomy by whatever method will not result in emptying of the bladder. Incidentally this type of bladder has not, in our experience, responded in any way to the administration of mecholin (figs. 6 and 7). To be sure, many such patients will survive in spite of large amounts of residual urine following prostatectomy. But the enfeebled old man under our present consideration may not.

It is our belief that all patients whose bladders fail to compensate after a fair trial of catheter drainage should be put on suprapubic drainage. In our own clinic this procedure might save 3 lives in 2 years; that doesn't seem like very many but it would reduce our mortality by 30 per cent.

Ann Arbor, Mich.

THE JOURNAL OF UROLOGY
Vol. 66, No. 3, Sept. 1951
Printed in U.S.A.

CARCINOMA OF THE PROSTATE

JAMES C. KIMBROUGH, COL., M.C., USA, AND ROBERT B. ROWE, MAJ., M.C.

From Surgical Service, Walter Reed General Hospital, Washington, D. C.

It is the scope of this paper to report the results of the analysis of the cases of carcinoma of the prostate at Walter Reed General Hospital during the 10-year period of 1940–1949. The incidence, diagnosis, treatment and follow-up are considered. Special attention is given to the selection of patients for radical operation and the results of this type of treatment.

INCIDENCE

During this decade, 78 patients with carcinoma and 435 patients with benign hypertrophy of the prostate were treated on the urological section. This number does not include the patients with benign hypertrophy of the prostate treated for other diseases and who did not come to the attention of the urologic section. Table 1 is a breakdown of the cases by years with the incidence and percentages.

AGE

The average for the 78 patients in the series was 65.8. The youngest was 43, the oldest, 89. Table 2 shows the age incidence for each decade.

The average age for the patients selected for radical prostatectomy was 65.2, the youngest was 51, the oldest, 74. The rectum was involved by direct extension in 1 patient. One patient had previous abdominal perineal operation for carcinoma of the rectum. Primary carcinoma of the bladder was present in 1 patient; 1 patient had had primary carcinoma of rectosigmoid.

DIAGNOSIS

Digital rectal examination gives the most valuable information prior to operation.[1] In the early cases the hard nodule is the first sign. As the carcinomatous process increases in size, the hardness extends, the gland becomes fixed and nodular and encroaches upon the membranous urethra. Later the induration involves the seminal vesicles and fills the intervesicular space. The rectal examination was negative for carcinoma in 6 patients and the proper diagnosis was established by pathological examination after operation. A positive diagnosis by rectal examination was proved erroneous by perineal biopsy at operation or pathological examination in 2 cases. The perineal biopsy has been used but often may be misleading unless the tissue for examination is removed from the cancer area. The biopsy specimen removed all the malignant tissue in one patient. The diagnosis was established or confirmed in transurethral resection in 18 patients, was negative in 2.[2] Perineal punch was positive in 2 cases and negabeen unavoidable but three of the cases fell into the group under present discussion. In retrospect one must conclude that these deaths might have been avoided by restricting our indications for transurethral resection and enlarging our utilization of preliminary puncture cystotomy drainage. To be sure, the safety of transurethral resection in these cases has been adequately demonstrated, for they survived the operation; but they finally went on to die from the complications of adynamic bladder dysfunction which we improperly treated. Prompt drainage, not early prostatectomy was indicated.

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[2] Hinman, F., Jr. and Hinman, F.: Occult carcinoma diagnosed upon transurethral resection. J. Urol., 62: 723–729, 1949.

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[1] Hinman, F.: The early diagnosis and radical treatment of prostatic carcinoma. Calif. Med., 68: 338–343, 1948.

[2] Hinman, F., Jr. and Hinman, F.: Occult carcinoma diagnosed upon transurethral resection. J. Urol., 62: 723–729, 1949.

The importance of the digital rectal investigation as a part of every physical examination in males over 40 cannot be overemphasized. During the period 1946–1949 inclusive, this phase of the examination was emphasized in the army physical examination. A sharp rise in the cases found and a great increase in the percentage amenable for radical extirpation followed these rectal examinations. The diagnosis was made by digital rectal examination alone in 6 cases. Three of these were confirmed later, one by autopsy, one by sternal puncture and one by cytological examination. These clinical diagnoses were verified by the experienced visiting staff and the degree of error is slight. Four of these patients had had operations (suprapubic 1, transurethral resection 3) because of benign prostate hypertrophy.

TABLE 1

YEAR	PTS WITH BPH	PTS WITH CARCINOMA	TOTAL	% OF TOTAL WITH CARCINOMA
1940	42	10	52	19.2
1941	49	3	52	5.7
1942	29	4	33	12.1
1943	32	4	36	11.
1944	26	4	30	13.3
1945	41	2	43	14.7
1946	50	7	57	12.3
1947	50	18	68	26.5
1948	59	14	73	19.2
1949	57	12	69	17.4
Totals	435	78	513	15.2

TABLE 2

AGE OF PATIENTS	NO. OF PATIENTS	PERCENTAGE
40–49	2	2.6%
50–59	19	24.3
60–69	33	42.3
70–79	18	23.0
80–	6	7.7

Differential diagnosis is not often difficult. Fibrosis following infection, calculi, and tuberculosis may be confusing. Sarcoma is rare and may require biopsy for final diagnosis; however, it is usually larger, softer and occurs in younger men.

TREATMENT

Palliative. Palliative treatment has been used in patients who showed evidence of metastases or local extension beyond limits of a cure with radical surgery. During the year 1940 there were 10 cases in the hospital, one of which was amenable for radical operation for cure and 9 for palliative therapy. At that time x-ray therapy, sedation and general care were the available measures. In 1941 castration and estrogen therapy were initiated (Huggins,[3] Herbst[4]). Five cases treated by these measures were bed-ridden with advanced metastases and suffering great pain. The effect of castration and estrogen therapy was dramatic for the relief of pain and the recession of metastases and size of prostate gland. These cases are all dead, and have been mentioned in previous reports by Dr. W. P. Herbst.[4]

In this series of 78 patients, 39 (50 per cent) *received only palliative therapy*. This therapy has given remarkable results in the relief of pain, recession of metastases, reduction in size of gland, and the prolongation of life. Thirty-one patients have been treated by castration, 8 of these had radical operation. A few have refused castration and have been treated by stilbesterol. Two patients, 81 and 85 years old, were treated by conservative perineal prostatectomy, because of age. Both are alive and well, 2 and 3 years respectively after operation. The most controversial phase concerning the use of estrogen therapy is the time when it should be begun. At this institution estrogen therapy plus castration is initiated as soon as it is established that there is extension of the malignant process beyond the possibility of surgical eradication.

Estrogen therapy and castration are used simultaneously. It has been established that castration plus estrogen therapy gives much better and more rapid results than estrogen therapy alone. It is realized that there is information that indicates that estrogen therapy eventually becomes ineffective and may have a definite therapeutic time span (Deming[5]) and that delaying this therapy until it is required for the relief of pain may give the patient greater longevity than its use in the early treatment. However, I believe that the earlier this therapy is begun the better will be the result.

Transurethral resection for the relief of obstructive symptoms and for diagnostic purpose has been used in 18 patients. The decrease in the size of the gland following estrogen therapy has reduced the number requiring transurethral resection for the relief of obstruction. Prefrontal lobotomy has been done in 3 cases with good results. Cystostomy drain was necessary in 2 patients. X-ray therapy has been practiced when other agents failed. The shortest duration noted for the effectiveness of this estrogen therapy was 18 months; the patient died of metastases, 2 years following castration and the use of stilbestrol. The response tive in 2. Cytologic examination has been done during the last year and was positive in 3. Cystoscopy gives little information except in advanced cases involving the trigone. Increase in the serum acid phosphatase has been noted with the presence of metastatic lesions. Androgen estimations have not been helpful. The symptoms, pain and urinary obstruction occur late. The first symptom in 2 patients was pain from metastatic lesion.

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[3] Huggins, C. and Hodges, C. V.: Studies on prostatic cancer. Cancer Research, 1: 293–297, 1941.

[4] Herbst, W. P.: Thoughts and observations on the relation of altered hormonal balance to prostatic malignancy. Urol. & Cut. Rev., 46: 691–694, 1942.

[5] Deming, C. L.: The correlation of clinical experience and heterologous growth of human prostatic cancer. J. Urol., 61: 281, 1949.

The importance of the digital rectal investigation as a part of every physical examination in males over 40 cannot be overemphasized. During the period 1946–1949 inclusive, this phase of the examination was emphasized in the army physical examination. A sharp rise in the cases found and a great increase in the percentage amenable for radical extirpation followed these rectal examinations. The diagnosis was made by digital rectal examination alone in 6 cases. Three of these were confirmed later, one by autopsy, one by sternal puncture and one by cytological examination. These clinical diagnoses were verified by the experienced visiting staff and the degree of error is slight. Four of these patients had had operations (suprapubic 1, transurethral resection 3) because of benign prostate hypertrophy.

TABLE 1

YEAR	PTS WITH BPH	PTS WITH CARCINOMA	TOTAL	% OF TOTAL WITH CARCINOMA
1940	42	10	52	19.2
1941	49	3	52	5.7
1942	29	4	33	12.1
1943	32	4	36	11.
1944	26	4	30	13.3
1945	41	2	43	14.7
1946	50	7	57	12.3
1947	50	18	68	26.5
1948	59	14	73	19.2
1949	57	12	69	17.4
Totals	435	78	513	15.2

TABLE 2

AGE OF PATIENTS	NO. OF PATIENTS	PERCENTAGE
40–49	2	2.6%
50–59	19	24.3
60–69	33	42.3
70–79	18	23.0
80–	6	7.7

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[3] Huggins, C. and Hodges, C. V.: Studies on prostatic cancer. Cancer Research, 1: 293–297, 1941.

[4] Herbst, W. P.: Thoughts and observations on the relation of altered hormonal balance to prostatic malignancy. Urol. & Cut. Rev., 46: 691–694, 1942.

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Bony metastasis has been affected very little. Metastases to the lung in some cases have disappeared.

Curative. Complete surgical excision of the involved structures is the only means that will effect a cure. Such treatment is made possible by early diagnosis. Radical prostatectomy has been carried out in 39 cases (50 per cent) in this series. The perineal approach was used in 38 and retropubic in 1. Table 3 shows the number and percentage of cases that had radical operation.

Usually the diagnosis was made by finding an isolated nodule. Following success of estrogen therapy in reducing the size of the gland the indications for radical perineal prostatectomy have been extended to include prostates decreased to operative limits by such therapy (Colston[6]). It is too early to evaluate the effectiveness of this type of treatment. In the patients who showed no extension beyond the parts removed by surgery no other therapy has been employed. In case the pathological specimen removed indicated that there was a definite evidence of extension of the malignancy beyond the surgical excision, castration was done and estrogen therapy begun soon after the radical operation.[7]

TABLE 3. *Radical perineal prostatectomy: Percentage of total carcinoma cases*

YEAR	PATIENTS TREATED WITH PERINEAL PROSTATECTOMY	% OF TOTAL CA. CASES FOR YR.
1940	1	10
1941	0	0
1942	0	0
1943	1	25
1944	2	50
1945	2	100
1946	3	42.9
1947	13	72.9
1948	9	64.3
1949	8	66.7
Totals	39	50

There have been 8 cases treated by castration in the series, one in 1944, one in 1947, 3 in 1948 and 3 in 1949. This increased number in recent years is evidence of the extension of the indication for radical surgery.

With the increased interest in early diagnosis the cases selected for radical surgical cure have increased markedly in the last three years. At the present time approximately 70 per cent of the patients are considered amenable to such surgery. This compares favorably with the optimism of Gutierrez.[8]

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[6] Colston, J. A. C. and Brendler, H.: Endocrine therapy in carcinoma of the prostate. J. A. M. A., 134: 848, 1947.

[7] Higbee, D. R.: Status of perineal prostatectomy today. J. A. M. A., 139: 3, 1949.

[8] Gutierrez, R.: New horizons in the surgical management of carcinoma of the prostate gland. Am. J. Surg., 68: 147, 1949.

RESULTS

The follow-up prior to 1946 has been incomplete and unsatisfactory. Two patients treated by castration and estrogen therapy because of wide local extension are without metastases, one 7 years after beginning the palliative treatment and one 6 years. Many of those with extensive metastases were bedridden and suffering great pain. These were relieved of pain and made ambulatory (reported by Dr. Herbst[4]). Bone metastases were reduced very little. The lesion disappeared from the chest in a few cases.

TABLE 4. *Patients treated by radical perineal prostatectomy with castration*

DATE	NO. PTS.
1940	0
1941	0
1942	0
1943	0
1944	1
1945	0
1946	0
1947	1
1948	3
1949	3
Total	8

TABLE 5. *5 Year report. Radical perineal prostatectomy results*

NO PATIENTS	L. & W.	WITHOUT METAS.	DEAD	UNKNOWN
6	4	?	?	2

TABLE 6. *Radical perineal prostatectomy since 1945*

POST-OP. OBSERVATION	NO OF PTS	L. & W.	DEAD OF CA.	DEAD OF OTHER CAUSES	UNKNOWN
4–5 years	2	1	0	0	1
3–4 years	3	1	1	0	1
2–3 years	13	10	1	2	
1–2 years	9	7	0	1	1
0–1 year	8	8	0	0	
Totals	35	27	2	3	3

Patients who were subjected to radical operation for cure have showed excellent results. Six cases had radical operation more than 5 years ago; 4 are living and well without metastases, 2 are unknown.

During the last 5 years of the period 35 patients had radical operation; 7 of these had castration and estrogen therapy because the pathological reports indicated extension beyond the operative excision. Twenty-seven are without metastases, 2 are dead of metastases at 2 and 3 years postoperative, 3 are dead of causes not related to carcinoma of the prostate and 3 are unknown. There has been no operative mortality or hospital death for the radical operations. One may not agree with Jewett[9] that it is a relatively simple procedure; but one can concur in his opinion that it is a safe operation attended by low mortality and little morbidity.

SUMMARY

The analysis of 78 patients treated for carcinoma of the prostate during the last decade is reported.

Palliative treatment, and the selection of patients for radical operation, are discussed.

The follow-up of the cases treated by radical operation is presented.

Radical operation was performed on 50 per cent of the cases during the 10 year period.

Curative surgery was carried out on 70 per cent of the cases observed during the last 3 years.

CONCLUSIONS

Castration plus estrogen therapy gives better results than either alone.

Castration and/or estrogen therapy preoperative has increased the range of curative operative procedures.

Early detection by rectal examination done as a part of the general physical examination has increased the range of operation for cure above 70 per cent of all cases.

The institution of castration and estrogen therapy as soon as local extension or metastasis is discovered is favored, as the palliative treatment of choice.

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[9] Jewett, H. J.: Radical prineal prostatectomy for cancer of the prostate. An analysis of 190 cases. J. Urol., **61:** 277, 1949.

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HISTOLOGICAL STUDIES OF CARCINOMA OF THE PROSTATE TREATED BY ESTROGEN

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From the Departments of Pathology and Urology, Jackson Memorial Hospital, Miami, Fla.

The dramatic and impressive successes attained by treating carcinoma of the prostate with orchiectomy and estrogen administration, as introduced and studied on a larger scale by Huggins and his co-workers, stimulated urologists and endocrinologists as well as pathologists.

Schenken and Burns, Heckel and Kretschmer, Moore and McLellan, and others have investigated the morphological changes which take place in a carcinoma of the prostate under the influence of stilbesterol. We may assume that studies dealing with morphological changes inflicted upon carcinoma of the prostate by orchiectomy and estrogen administration are scarce as compared with other investigations of this treatment because the therapeutic effect takes place within such a short period of time, though transitory in the majority of cases, that the primary focus practically disappears. Furthermore, strangely enough, bone metastases developing in the course of the carcinoma of the prostate are mainly studied by roentgenologists, while pathologists, with few exceptions, are satisfied with describing them grossly, in spite of their striking response to estrogen treatment. It is generally assumed that the vast majority of these metastases are osteoplastic rather than osteoclastic in type.

Studying hundreds of prostates surgically removed or obtained from autopsies for the past 6–8 years, we noticed so-called squamous cell metaplasia (the transformation of columnar or cuboidal epithelium into squamous epithelium) more frequently than expected, no matter whether these glands showed benign hypertrophy, with or without inflammatory changes, prostatic infarcts, calculi, or carcinoma. A number of these cases had received stilbesterol for one reason or another. This observation suggested studies on the histological influence of stilbesterol on carcinoma of the prostate and its metastases.

In spite of the large supply of material relative to the matter, it was quite difficult to select cases representing similar response to estrogen in different pathological conditions. Our analysis and our conclusions are based on the following already established facts:

1. During intra-uterine life, solid plugs of squamous cells bud from the urethra and are gradually transformed into columnar-cell lined glands, the latter process starting immediately after birth. (Schlachta, Stieve, Brody and Goldman, etc.). It is generally assumed that maternal estrogen, conveyed to the fetus by way of the placenta, is responsible for the formation of these squamous cell plugs. As established by Papanicolaou and Shorr and others, in animals estrogen administration produces hornification in the vagina of the Rhesus monkey. Stieve showed

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Read at annual meeting, American Urological Association, Washington, D. C., May 30, 1950.

that the development of the prostate takes place in two waves, the first ending approximately with the first year of life, the second ending around the eleventh, with an interval of rest of several years. Both of these phases start with the formation of plugs of squamous cell epithelium. As maternal estrogen is not available at this time, it must be assumed to be of adrenal origin; similar reflexions may also apply to the well established fact of estrogen elimination in male adults.

2. Numerous authorities observed squamous cell metaplasia in the urethra, the utriculus, the prostatic ducts and glands in different animals after the application of estrogen (Lacassagne, Zuckerman, Moore, Huggins, Clark and many more).

3. Myelofibrosis, osteosclerosis and endostal changes producing a pagetoid picture (Gardner and Pfeiffer, Erf and Herbut) observed after estrogen administration.

4. Squamous cell metaplasia in the prostate of man without estrogen administration.

a) Associated with or following infarcts of the prostate.

b) In chronic irritations and inflammations of the acini. Here it occurs often together with corpora amylacea. Also in these cases we have to assume that the estrogen is delivered by the cortex of the adrenals.

5. Occurrence of squamous metaplasia in carcinoma of the corpus of the uterus, referred to as cancroid of the uterus. It is supposed to occur in long standing adenocarcinomas or in those which had undergone local treatment. Squamous cell metaplasia is very frequent in cervicitis and endocervicitis. Though this is usually attributed to irritation and inflammation, numerous authorities hold hormonal (estrogen) influences responsible (Hofbauer, Schiller, Hintze, Hinselmann, etc.). We agree with this opinion and would also like to claim the same factor to be responsible for the metaplastic change which transforms an adenocarcinoma into a cancroid of the uterus.

CASE REPORTS

The cases we have selected for demonstration represent the following types: One case was clinically misdiagnosed as carcinoma and the patient was given stilbesterol, then operated on; the second case was one of carcinoma, and the patient underwent estrogen treatment followed by surgery; the third case was was one of carcinoma, in which the patient was subjected to orchiectomy; he has been on permanent stilbesterol treatment for years; and repeated biopsies were obtained and transurethral resection performed 6 times; finally, the fourth case deals with a carcinoma in which the patient was treated with estrogen, exhibited some metastases, died and came to autopsy.*

Case 1. A 72 year old man complained of burning sensations and frequency which made him suspect that he was suffering from prostatic disease. Rectal examination revealed a firm prostate gland and the diagnosis of carcinoma of the prostate was made. Before performing radical perineal prostatectomy, the patient received 5 mg. stilbesterol daily for 63 days. The gross examination of the prostate revealed small cysts and a few small calculi, but no evidence of carcinoma; microscopically numerous areas of metaplasia were noticed, characterized by transformation of the columnar epithelium of the prostatic glands and ducts into squamous epithelium, in several cases encroaching corpora amylacea, which were very numerous. The same case also exposed many inflammatory areas and especially infarcts with metaplastic changes at the periphery. In close relation with the necrotic areas of the infarcts, we found giant cells stimulated by disintegrating corpora amylacea, which act like a foreign body, a reaction in the prostate often mistaken for tuberculosis.

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* We are indebted to Drs. E. Clay Shaw and James J. Nugent of Miami, Florida for the use of the histories of the first 3 cases.

Though this type of metaplasia, without doubt, also occurs from time to time in inflammatory lesions and in prostatic infarcts, it can be shown by one of our slides that estrogen played a predominant part in the formation of this metaplasia, inasmuch as the utriculus prostaticus, which is extremely sensitive to hormonal influences, showed marked squamous metaplasia. This proves that, to a large extent at least, the metaplastic changes were based on estrogen administration.

Case 2. In a 75 year old man carcinoma of the prostate was diagnosed clinically and confirmed pathologically. The patient took 5 mg. of stilbesterol daily for 60 days. This was followed by perineal prostatectomy. Here also histological examination revealed a moderate amount of corpora amylacea. Carcinoma of the prostate was still present, though in a very minor degree, and very marked squamous cell metaplasia, together with extensive fibrosis could be noted throughout the whole gland, including the utriculus. In both these cases the connection between metaplasia and estrogen administration is not conclusive but very probable.

Case 3. A 75 year old man in whom carcinoma of the prostate had been diagnosed clinically underwent orchiectomy and transurethral resection in 1941 at the Cleveland Clinic. Between 1942 and 1946, patient had 5 more transurethral resections in different clinics in the north, and was first seen in Miami in 1946. He has been given stilbesterol prior to this time, but it caused nausea and he therefore did not take too much of it. In January 1946, he was again started on stilbesterol, the dose of which was varied from 5–15 mg. daily. Since then he has taken it almost continuously during the past 4 years. X-ray pictures of bones and chest, taken as late as November 1949, did not show evidence of metastases. Also, examination of a plain urogram made at this time was negative. This case is especially important as its course was followed by numerous biopsies. Their study shows how the pattern of the carcinoma changed under the influence of the different therapeutic procedures. The first biopsy* we had accesss to carries the date of May 30, 1942. The pathological diagnosis at that time was adenocarcinoma of the prostate. The second biopsy* was made on April 21, 1943, and the diagnosis, according to Dr. Hazard, was carcinoma simplex of the prostate. We compared these two biopsies and could see how the adenocarcinoma,

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* For the use of this material we are indebted to Dr. T. B. Hazard of Cleveland, Ohio.

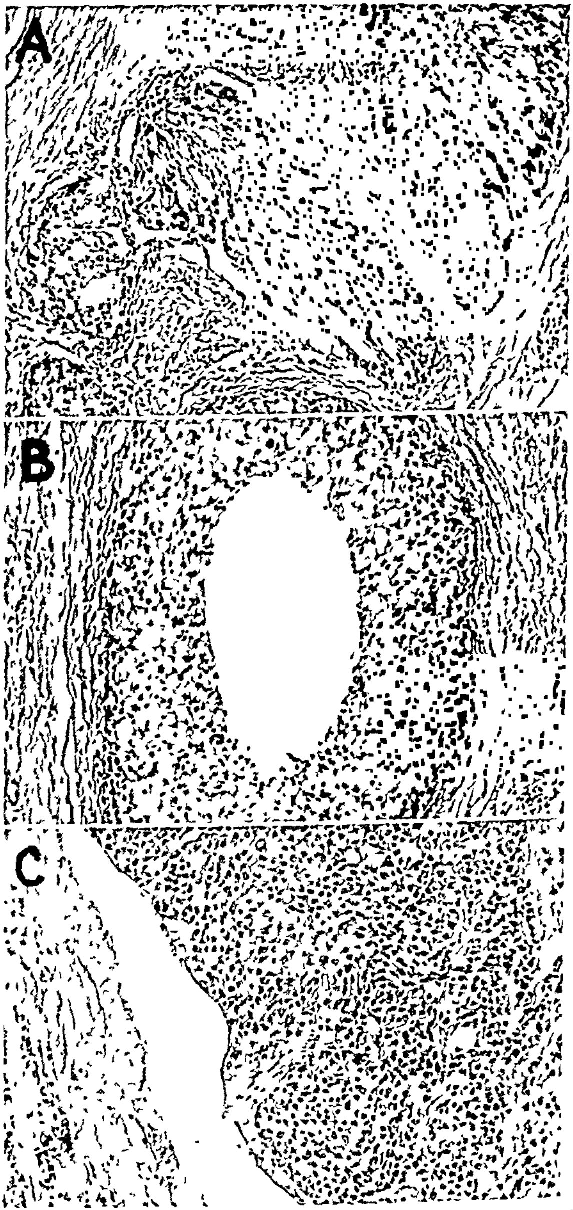


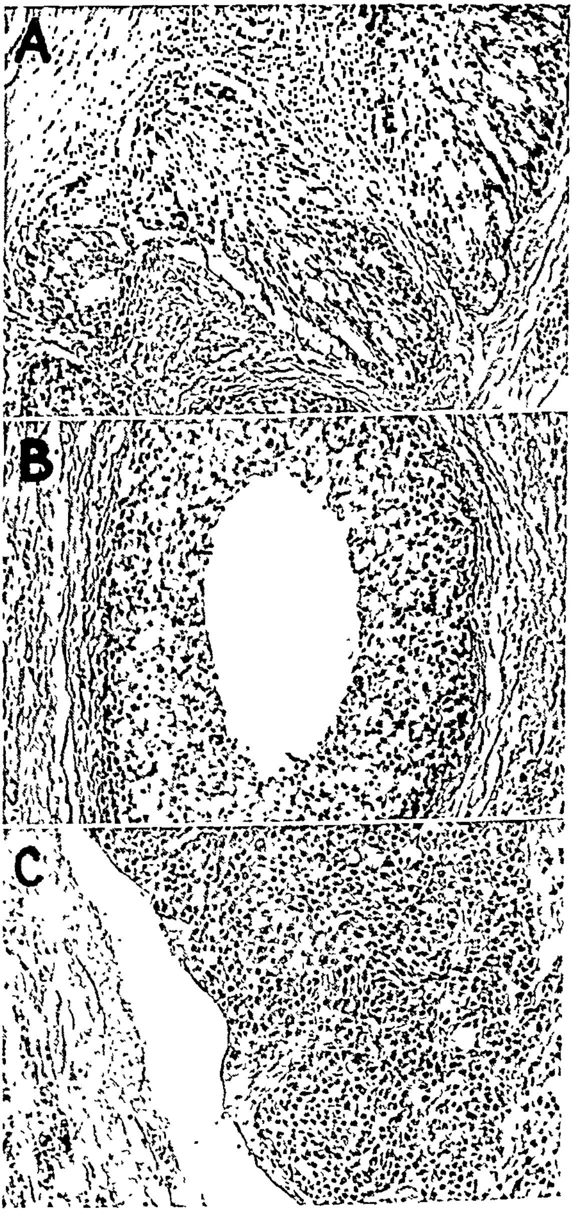
FIG. 1. Case 3. *A*, prostate (× 86) Adenocarcinoma First biopsy taken shortly after diagnosis was made *B*, prostate (× 100). Carcinoma simplex Second biopsy taken about one year after first one Patient had undergone orchiectomy and was receiving stilbesterol. No glandular formations present any more, vesicular cell complexes *with small nuclei* (as described by Schenken and Burns). *C*, prostate (× 86) Solid carcinoma (squamous cell grade 4). Third biopsy taken 1949, about seven years after first one. Patient constantly under stilbesterol administration.

present in the first slide (fig. 1, *A*), in the second becomes replaced gradually by a somewhat different type of carcinoma, whose cells remind one of those vesicular cells with small nuclei, which Schenken and Burns claim to be characteristic for the influence of stilbesterol (fig. 1, *B*). Besides these, there were areas of tumor cells of still another type which from then on became prevalent.

The first biopsy taken and examined by us was performed on February 11, 1949. Here we found tremendous areas of necrosis, associated with islands of neoplastic tissue, extremely poorly differentiated, which were arranged in solid strands and beams. In several instances, one had the impression of a very poorly differentiated squamous cell type of carcinoma (fig. 1, *C*). Along with this material, we also obtained pieces of prostatic tissue not yet involved by carcinoma, and in which we noticed marked metaplasia and formation of epithelial pearls, changes which had not been seen in the first two biopsies. And finally sections obtained from a massive transurethral resection of a large tumor, performed on November 18, 1949, reveal the same picture, only more outspoken, with predominant islands of very immature tumor cells, associated with marked mature squamous cell metaplasia of the prostatic part of the urethra and of the noncarcinomatous part of the prostate. Analyzing this case, it appears to be very likely that under the influence of stilbesterol the carcinoma changed its aspect completely, inasmuch as the adenocarcinoma was converted into a poorly differentiated squamous cell carcinoma. These changes are strikingly similar to those which we mentioned previously and which occur in certain adenocarcinomas of the corpus uteri, probably induced by estrogen. Though the long survival in this case seems rather surprising, we may quote Flynn, who reported a case of carcinoma of the prostate of 12 years' duration. With regard to its histological pattern, our case shows some similarity to that published by Graves and Cross.

Case 4. This case is of extreme importance, as in it we attempt to show that estrogen not only changes the pattern of the primary tumor, but also produces metaplasia in its bone metastases, apart from well known fibrosis and osteoplasia. To our knowledge, this has not been described before.

A 60 year old man was admitted to the Jackson Memorial Hospital on April 24, 1948. His symptoms and complaints, as well as examinations, indicated a carcinoma of the prostate with metastases in the bones, associated, according to x-ray reports, with Paget's disease. At this time the serum acid phosphatase was 2.2 units and the serum alkaline phosphatase was 23.4 units. One month later the serum acid phosphatase was 266.6 units and the alkaline phosphatase was 17.5 units. The patient's serum acid phosphatase was so high that the figure is not reliable. The serum calcium was 10.2 mg. The patient was given 10 mg. stilbesterol daily, was discharged to a convalescent home on June 6, 1948, and was re-admitted to the hospital on September 3, 1948. At this time the acid phosphatase was 196.7 units, the alkaline phosphatase was 9.8 units. On September 16, the patient was placed on 10 mg. stilbesterol daily and on October 9 (24 days later) the alkaline phosphatase was 21.6 units and the acid phosphatase 11.7 units. On November 8, the patient was discharged at his wife's request. Six days later he was readmitted because of gross hematuria of 3 days' duration, and oliguria and anuria of 1 days' duration. He was very emaciated, was in semi-coma; the serum acid phosphatase at this time was 5.1 units, the alkaline



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The patient came to autopsy with the clinical diagnosis of metastasizing prostatic carcinoma, Paget's disease, cachexia and pathological fracture of the right femur.

Abstract of the autopsy findings: "Thorax revealed a deformity of the left thoracic cage, due to nodular masses involving almost the entire substance of the first and second left ribs in their posterior parts. It also showed nodular irregularity of the fourth and sixth ribs in the posterior midscapular line. Macroscopic changes compatible with osteoplastic metastases in the form of irregularly shaped, large, firm ebonized patches were also seen in the sternum, vertebrae, long bones, etc. The skull showed marked thickening of the dome throughout, with loss of normal diploic spaces, except in scattered areas. In addition, there were two almost circular punctured areas of 1½ cm. diameter in the fronto-parietal section. Both kidneys presented all the signs of arterio- and arteriolosclerosis with superimposed multiple, greyish-yellow subcortical abscesses, marked pyonephrosis, ascending pyelonephritis, purulent hemorrhagic cystitis. The prostate was rather firm in consistency, hardly enlarged, and was not difficult to dislodge."

Of the histological findings, only those pertaining to the prostate, the metastatic and other changes in the bones and, to some extent, those in the kidneys, shall be reported here. The primary carcinoma in the prostate presented itself in form of remnants of islands of adenocarcinoma, the single glands of which were lined with very dark pyknotic cells with large nucleoli (fig. 2, *A*). In several areas this glandular formation became indistinct, the lumen disappeared and there seemed to be a tendency to plug formation, similar to that seen in certain types of squamous cell carcinoma (fig. 2, *B*). Only the findings in the metastatic lesions in the bones, which we shall discuss later, suggested to us that metaplasia from one type of carcinoma into another was also taking place in the prostate. This assumption was borne out by the facts that serial sections of the plugs proved their solidity. All these scattered islands of carcinoma were lodged in marked fibrosis, rather rich in cells. Inflammatory changes of interglandular areas, small areas of necrosis (infarcts) and a moderate amount of corpora amylacea, together with deposits of lime salts were also noted.

Typical squamous cell metaplasia, in no way related to the tumor formation itself, completely mature in type, was found in the lining of the prostatic part of the urethra, from where benign plugs penetrated into the surroundings, in the utriculus and in acini, some of which contained corpora amylacea (fig. 2, *C*).

Though peculiarities of the metastases represent the most important findings in our analysis, we shall first describe the concomitant changes in bone and bone marrow which are also ascribed to estrogen, but which are already well known. Though osteoplastic changes are predominant, osteoclastic manifestations are present too, both leading to osteosclerosis and osteofibrosis, respectively. Islands of tumor are surrounded by osteoid or osteospongious, newly formed bone spicula. A large amount of connective tissue was present, which belongs to the fibrotic bone marrow, often referred to as localized fibrous ostitis. This connective tissue produces bone. All these processes, old necrosis, osteoclastic,

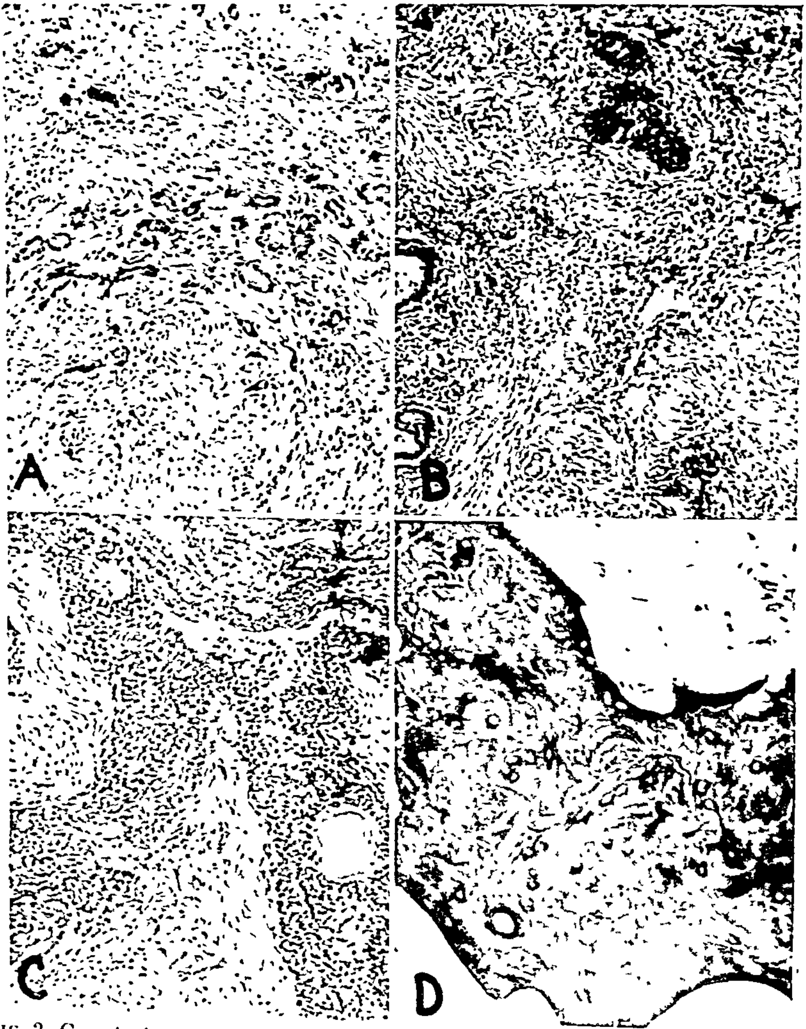

FIG 2 Case 4 *A*, prostate (× 86). Adenocarcinoma plus fibrosis. *B*, prostate (× 82). Adenocarcinoma, fibrosis and plugs of squamous cell carcinoma on right (metaplasia). *C*, prostate (× 100) Marked benign squamous cell metaplasia in areas of prostate not involved by carcinoma *D*, bone (× 88). Pagetoid reaction, represented by newly formed bone (notice mosaic pattern produced by lamellae of newly formed bone).

as well as osteoplastic changes, had destroyed the original bone structure completely. In areas where the old spongiosa became resorbed but was not completely substituted by newly formed spongiosa, the bone marrow accepted a fibrous appearance and was infiltrated with carcinomatous formation. In some areas the osteoplastic activity was so strong that the destructive character produced by the carcinomatous infiltration was not detectable. This could be demonstrated especially well in the corpora of the vertebrae and in the skull,

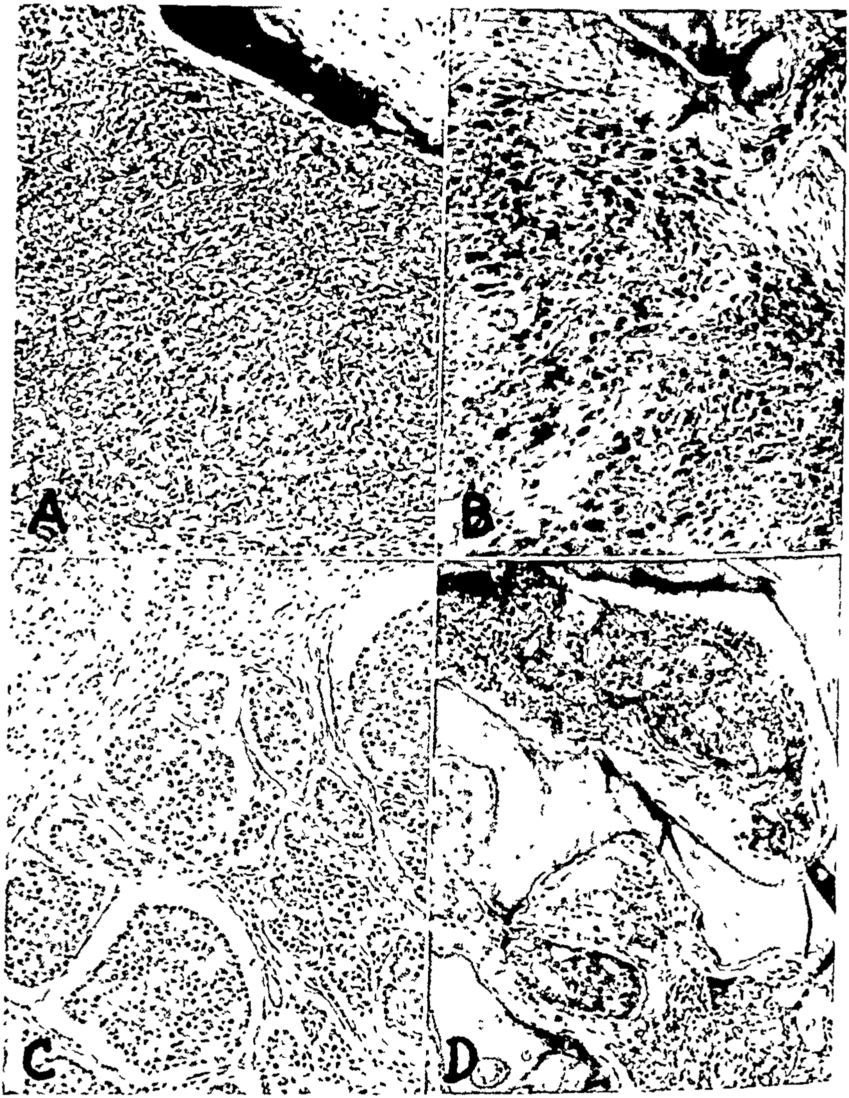

FIG. 3. Case 4. *A*, bone marrow (× 86). Localized osteofibrosis, imitating tumor formation, often associated with deposits of hemosiderin and lipoid storing cells (pseudoxanthofibroma). *B*, bone marrow (× 100). Osteofibrosis, altered tumor cells compressed by connective tissue (desmoplastic reaction). *C*, bone marrow (× 100). Plugs of squamouscell carcinoma. *D*, bone marrow (× 100). *Metastasis of adenocarcinoma (in upper half of picture), squamous cell carcinoma, result of local metaplasia (right lower corner) and transition from adeno to squamous cell carcinoma (to left of island of squamous cell carcinoma).*

where carcinoma could not be discovered under the microscope. The result of all these activities was a picture rather typical of Paget's disease (pagetoid reaction). It may be considered a sort of self cure (fig. 2, *D*).

Apart from this pagetoid reaction, another tissue change should be mentioned. It consisted of extensive fibrosis which was noted, not only beneath the endostium of the long bones, but also in other areas. This fibrosis was very rich in cells and in newly formed blood vessels. Extensive old and new hemorrhages were found in these regions; the former were characterized by such massive accumulation of hemosiderotic pigments that only special staining reactions prevented us from mistaking it for malanin. Some giant cells (osteoclasts?) could be seen around these hemorrhages. In some instances these patches of fibrosis showed sclerotizing features associated with scarce deposits of lipoid storing cells. The whole picture reminded somewhat of localized xantho-fibrosis (fig. 3, *A*).

Studies of the bone marrow, not involved by osteosclerosis or fibrosis, revealed marked cellular hyperplasia of functioning bone marrow. Nevertheless, within this hyperplasia megakaryocytes were somewhat scanty. We also searched for extramedullary hematopoesis in all the organs and found it only to a minor degree in the adrenals. So much for the bone changes with and without relation to the carcinomatous metastases.

A most peculiar behavior was exhibited by the metastases themselves. Very careful serial sections showed two different types of carcinomatous structure: one, the typical adenocarcinoma with all the characteristics of carcinomatous glands; and the other, typical plugs of rather poorly differentiated squamous cell carcinoma. These plugs were first considered to be tangential sections of the periphery of the glands, but serial sections revealed them to be solid and to have all the characteristics of squamous cell carcinoma. In some slides there was only adenocarcinoma, in others only squamous, and in others again both types could be seen. None of the bones examined showed preference for one type or the other. Finally, we discovered some areas where a transitional phase between the squamous cell metaplasia and true adenocarcinoma could be seen (fig. 3, *B*, *C*, *D*).

The histological findings on kidney and pelvis corresponded with our gross impression, as all characteristics of an ascending purulent abscess forming pyelonephritis could be noticed under the microscope.

DISCUSSION AND CONCLUSIONS

It was demonstrated by Gardner and Pfeiffer that estrogen may be the cause of fibrosis of the bone marrow. The same authors, as well as Miller, Orr and Pybus, claimed that the preponderance of estrogen in a case of myelofibrosis was due to an inability of the liver to conjugate the estrogen in normal quantities. Estrogens, however, may function in a variety of ways, as proved by Huggins in 1943, who showed that following estrogen therapy "in 4 patients extensive osteous metastases have completely disappeared according to radiographic examination." This type of regression is possibly similar to that seen in Paget's disease when the latter is healing, as proved by Jaffe. He expresses this process of healing as "a tendency to the return of a normal appearance of the bone and bone marrow. The fibrous marrow becomes replaced by more lymphoid and fatty marrow." The mechanism for the development of such a secondary myelofibrosis was brought about in connection with the occlusion of blood vessels of

the marrow, due to infarction, either by tumor cells or by other obstructing material.

Of much greater importance, in our opinion, is the evidence of squamous cell metaplasia, not only in the primary tumor but also in the metastases, following estrogen medication. One is hardly able to claim, as is done for the prostate itself, that this metaplasia in the bone metastases of a carcinoma of the prostate is spontaneous, due to irritations, inflammation or infarction. With regard to our previous statement and to experiments in this matter, we consider it very likely that the squamous metaplasia in bone metastases of carcinoma of the prostate may be a direct consequence of estrogen administration.

Summarizing, we may say that the presence of squamous cell metaplasia in a prostate may be qualitatively and quantitatively an indication of the amount of estrogen substances of the carrier. Such an assumption may answer the question why certain individuals exhibit inflammation, infarcts, corpora amylacea, irritation, etc., with metaplasia, while others having a lower estrogen level do not show such concommitant squamous cell metaplasia. We have to admit that we do not know whether or not this estrogen is of adrenal origin. It is conceivable that different types of squamous cell carcinoma in males and females may show some relation to the estrogen present in the carrier. A very interesting example to prove such a possibility would be the analysis and examination of so-called cancroids of the uterus which are, as already mentioned, carcinomas of the uterus of long standing in which transition from adeno- into squamous cell carcinoma has taken place. Is it not conceivable that such a transition, or better, such a metaplasia may take place under the influence of an abundance of estrogen in the female?

To prove this theory, we cannot expose a woman suffering from adenocarcinoma to a large amount of estrogen and wait to see whether she develops a cancroid of the uterus. However, it would be interesting to make such studies in animals, in which spontaneous adenocarcinomas of the uterus do occur. Certain experiments in mice, guinea pigs, etc., encourage such an assumption.

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REFERENCES

Brody, H. and Goldman, S.: Arch. Path., **29:** 491, 1940.
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Gardner, W. V. and Pfeiffer, C. A.: Proc. Soc. Exp. Biol. and Med., **38:** 599, 1938.
Graves, R. C. and Cross, T.: J. Urol., **51:** 59, 1944.
Heckel, N. J. and [illegible] .A.M.A., **119:** 1087, 1942.
Hinselmann: Hdb. [illegible], vol. 6, p. 1, Muenchen, 1930.
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Hofbauer, J.: Zentralbl. f. Gynaek., **55:** 428, 1931.
Huggins, C.: New York State J. Med., **43:** 519, 1943.
Huggins, C.: Harvey Lectures, 1946-1947.
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Lacassagne, A.: Compt. rend. Soc. Biol., **113:** 580, 1933.
Lacassagne, A.: Compt. rend. Soc. Biol., **120:** 1156, 1935.
Lacassagne, A.: Compt. rend. Soc. Biol., **121:** 697, 1936.
Lacassagne, A. and Villella, E.: Comp. rend. Soc. Biol., **114:** 870, 1933.
Miller, E. W., Orr, J. W. and Pybus, F. C.: J. Path. and Bact., **55:** 137, 1943.
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Moore, R. A.: Surgery, **16:** 152, 1944.
Moore, R. A.: Endocrinology of Neoplastic Disease. Oxford Med. Publ., 1947.
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Papanicolaou, G. N. and Shorr, E.: Am. J. Obst. and Gynec., **31:** 806, 1936.
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Schiller, W.: Arch. F. Gynaek., **133:** 211, 1928.
Schlachta, J.: Arch. Mikrosk. Anat., **64:** 405, 1901.
Shorr, E. and Papanicolaou, G. N.: Proc. Soc. Exp. Biol. and Med., **41:** 629, 1939.
Stieve, H.: Hdb. d mikrosck. Anat. d. Menschen., 1930.
Zuckerman, S.: Lancet, **1:** 435, 1937.
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Zuckerman, S.: Biol. Revs. **15:** 231, 1940.
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Graves, R. C. and Cross, T.: J. Urol., **51**: 59, 1944.
Heckel, N. J. and Kretschmer, H. L.: J.A.M.A., **119**: 1087, 1942.
Hinselmann: Hdb. d. Gynaek (Stoeckel), vol. 6, p. 1, Muenchen, 1930.
Hintze, O.: Zbltt. f. Gynaek., **52**: 2209, 1928.
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I should like to have Colonel Kimbrough tell us what anesthesia he used. For all perineal operations we have been exceedingly pleased by our results with continuous caudal, using a malleable needle and 80 cc of 1 per cent novocaine solution, added to or not as necessary, usually not.

Colonel Kimbrough is to be congratulated upon his zero mortality rate, as well as upon his optimism and his courage.

DR. J. HARTWELL HARRISON (Boston, Mass.): I wish to state that we have followed the conviction during the last 5 years that, in attacking cancer of the prostate, it is necessary for us to utilize both the biologic and the surgical means at our disposal. Perhaps because we are yet neophytes, we still think in terms of cure of cancer of the prostate, and at the same time we should profit by the healthy restraint of philosophical remarks such as those made by Dr. Edwin Davis.

An analysis of 100 consecutive carcinomas of the prostate admitted to the Peter Bent Brigham Hospital during the years from 1946 to 1949 has been made by Dr. Eugene Poutasse, now at the Cleveland Clinic, and myself. I should like to show briefly a summation of certain aspects of these data which are to be submitted later for publication.

(Slide) This first slide shows us the age distribution, which is not unusual. You will see that it corresponds very closely to those that Colonel Kimbrough has shown us and that 75 per cent of these patients are found in the seventh and eighth decade.

(Slide) It is seen that only 60 of these patients were admitted to the hospital with a diagnosis of carcinoma of the prostate; admitted for other reasons, 39; and in 11 of these patients, the diagnosis of carcinoma was only made on study of sections by the pathologist after a routine prostatectomy when the preoperative diagnosis had been benign hyperplasia. The process was recognized as localized within the gland in 16 cases and in 3 others was thought to be localized but found to be beyond the capsule of the gland at operation. In 10 cases, the diagnosis was made on permanent section; in one instance a frozen section disclosed previously unsuspected carcinoma and a total prostatectomy was done. Regional distribution of the disease, that is, neoplasm extending beyond the prostate gland through the region of the seminal vesicles and laterally, was present in 45 cases, without distant metastasis being demonstrable; in 29 cases distant metastasis was demonstrable.

(Slide) Efforts at combined therapy are summarized here. We have utilized castration plus estrogenic therapy in all cases, where possible. This was in 51 cases; castration alone in 18; estrogen alone in 18; and neither castration nor estrogens in 13 patients.

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DISCUSSION

DR. EDWIN DAVIS (Omaha, Neb.): A critical analysis of methods and results as Colonel Kimbrough has presented is always helpful, and serves as food for thought.

I mention first a matter of terminology. In discussing with patients or physicians the only procedure which offers any prospect of cure of early prostatic cancer, I believe the term total prostatectomy is much to be preferred to radical prostatectomy, by reason of the far less formidable implication of the former. Rather than castration, I have always used the term orchiectomy referring to the shelling out of merely the parenchymatous portion of the testicle, leaving in situ the tunic, albuginea and cord which together make up quite a respectable and presentable little mass.

I believe that most of you will agree that prostatic cancer, by reason of its slow rate of growth, its response to anti-androgenic palliation and its amenability to transurethral resection, and occasionally to cure by complete excision, may be viewed as the most benign of all malignancies involving vital organs. Were I doomed to cancer, as I may be, and as many of us undoubtedly are, and had I my choice, I should choose cancer of the prostate.

I have nothing but praise for Colonel Kimbrough who I am sure will not disapprove of my surprise that his percentage of prostatic carcinoma patients amenable to total prostatectomy should be so inordinately high. Colby has reported that "only about five per cent of patients with prostatic cancer . . . fulfill the conditions for radical surgery." My own percentage is certainly no higher; the obvious reason for this low percentage being that early stage prostatic cancer is usually quite symptomless, and seldom comes to the attention of the urologist, unless because of co-existing, obstructing benign hypertrophy, or unless discovered by the alert internist during the course of a routine general physical examination, of which digital rectal examination should always be an essential part.

It would seem at first that Colonel Kimbrough's surprisingly high percentage (50 per cent during the entire 10-year period, and 70 per cent "at the present time") of prostatic cancer patients treated by total prostatectomy, may be explained in part by rigid Army regulations including "digital rectal investigation as a part of every physical examination in males over 40." This, however, is not the case, since his 15 per cent reported incidence of malignancy among prostatics under treatment at the Walter Reed Hospital during the last decade is somewhat lower, rather than higher, than reported by other clinics. In addition to Colonel Kimbrough's courage and optimism, the chief factor in this high percentage, therefore, must have been the including of "prostates decreased to operative limits" by orchiectomy and/or estrogen therapy, as advocated by Colston in 1947; also recently by Gutierrez, who likewise has reported a very high percentage of total prostatectomy. Here again arises the question of terminology. We must distinguish between clinical prostatic malignancy and malignancy reported by the pathologists, who, by including microscopic evidence, have boosted this figure as high as 40 per cent of men coming to autopsy beyond the age of 50.

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An analysis of 100 consecutive carcinomas of the prostate admitted to the Peter Bent Brigham Hospital during the years from 1946 to 1949 has been made by Dr. Eugene Poutasse, now at the Cleveland Clinic, and myself. I should like to show briefly a summation of certain aspects of these data which are to be submitted later for publication.

(Slide) This first slide shows us the age distribution, which is not unusual. You will see that it corresponds very closely to those that Colonel Kimbrough has shown us and that 75 per cent of these patients are found in the seventh and eighth decade.

(Slide) It is seen that only 60 of these patients were admitted to the hospital with a diagnosis of carcinoma of the prostate; admitted for other reasons, 39; and in 11 of these patients, the diagnosis of carcinoma was only made on study of sections by the pathologist after a routine prostatectomy when the preoperative diagnosis had been benign hyperplasia. The process was recognized as localized within the gland in 16 cases and in 3 others was thought to be localized but found to be beyond the capsule of the gland at operation. In 10 cases, the diagnosis was made on permanent section; in one instance a frozen section disclosed previously unsuspected carcinoma and a total prostatectomy was done. Regional distribution of the disease, that is, neoplasm extending beyond the prostate gland through the region of the seminal vesicles and laterally, was present in 45 cases, without distant metastasis being demonstrable; in 29 cases distant metastasis was demonstrable.

(Slide) Efforts at combined therapy are summarized here. We have utilized castration plus estrogenic therapy in all cases, where possible. This was in 51 cases; castration alone in 18; estrogen alone in 18; and neither castration nor estrogens in 13 patients.

Nineteen total prostatectomies were done in which it was possible to remove the vesicles along with the prostate; 16 of those patients are surviving 2 years after operation, and of those 16 only 3 have definite evidence of metastasis.

Of the group of 29 patients having partial prostatectomy, 10 had enucleation for benign hyperplasia of the prostate. For the remaining 19 of that group palliative partial prostatectomy was carried out. Only 14 of the patients of this group are living.

(Slide) It is obvious that this is a very early survey and the number of cases is small, but I thought it would be interesting to note that there are 62 of these patients living at the present time, 29 who have died of carcinoma, and 9 who have died of other causes.

Colonel Kimbrough is to be congratulated on the vigorous attempts he has instituted to combat cancer of the prostate and for the successful execution of such a high percentage of radical prostatectomies.

Dr. Thomas F. Howley (New York, N. Y.): A review of the answers to a questionnaire received from 125 members of this Association, with regard to treatment of cancer of the prostate, revealed agreement with what we have heard in these papers and varied on only two points: 1) that early carcinoma of the prostate is seen too seldom; and 2) that hormonal therapy, while it will not cure carcinoma of the prostate, will give the patient a longer comfortable life and shorter terminal downhill stage.

The extent of disagreement on the methods of treatment of cancer of the prostate can be judged by just these few figures briefly given. Forty-seven members favor administering estrogen to all cases of carcinoma of the prostate. Twenty-four men believe that estrogen and orchiectomy are indicated in all cases of carcinoma of the prostate. Twenty-three men consider metastasis an indication for orchiectomy. Sixteen performed orchiectomy for metastatic pain.

For the inoperable cases, 46 men favor estrogen and orchiectomy early. Ten men prefer estrogen and orchiectomy later. Eighty-five continue estrogen therapy after orchiectomy. Twenty-five give estrogen therapy only after orchiectomy and only upon return of symptoms or where there has been no effect from the orchiectomy.

Some few members favor doing nothing for their patients until symptoms appear. Then there are some men who administer large doses of estrogen, giving from 1 to 3 hundred milligrams daily, one man giving as much as 1 thousand milligrams daily.

We at St. Vincent's Hospital believe, with Colonel Kimbrough, that the diagnosis of carcinoma of the prostate is to be made clinically, that is by the rectal finger. We prefer to give the patient in a questionable case of carcinoma of the prostate a therapeutic course of estrogens rather than open an otherwise closed lesion by performing a perineal exposure, needle biopsy, or transurethral resection to obtain a specimen.

We explain the difference of opinion of all these men expressed in this questionnaire by the fact that the response to treatment of carcinoma of the prostate varies. Until the cause for this is discovered, there will be these differences of opinion.

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TREATMENT OF CARCINOMA OF PROSTATE

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Carcinoma of the prostate is being attacked in the following manner: 1) early diagnosis with radical removal of the prostate; 2) endocrine control with palliative surgery calculated to relieve the patient of urinary obstruction and osseous pain.

Recent improvements in the techniques of anesthesia, blood transfusion, radical prostatectomy, treatment of infections, etc. have increased tremendously the possibilities and safety of radical surgery. On the other hand, since 1941 and the work of Huggins, Munger, Herbst, Scott and Vermeulen, Nesbit, and many others, the possibilities of endocrine control of this neoplasm, either as an adjunct to surgery or as a complete therapy in itself, have been emphasized. It has been shown that, with endocrine treatment, patients with carcinoma of the prostate could be improved clinically: gain weight, return to normal activities, have dramatic relief from metastatic pain, show reduction in size of the prostate and radiologic evidence of metastatic regression. These two, in some respects divergent and yet in other respects complementary methods of attack, raise questions with regard to the paths along which one should go in the treatment of these patients as they present themselves at the present time.

It is the purpose of this report to outline a rational therapy (for these patients) upon the basis of a series of 854 patients with carcinoma seen at the University Hospitals from January 1, 1926, to July 1, 1945. Every one of these patients has been followed 5 years or more. In addition to a study of this series of patients, a study of individual cases that have been followed less than 5 years, and the results of other observers reported in the literature form the basis of the indications for the treatment to be outlined.

When patients with carcinoma of the prostate present themselves to the physician they may be classified as follows: 1) the cancer may be limited to the prostate; 2) the cancer may extend beyond the prostatic capsule but no metastases may be evident; 3) definite metastases are present.

What should be done with the patients in these groups?

Of the 854 patients of our series 281, or 33 per cent, fell into the first group. From a comparison of table 1 (which shows the 5-year survivals in Nesbit and Baum's series), figure 1 (which gives the 5-year survivals in our cases and those of the radical prostatectomy series of Belt and Colston), table 2 (which gives the 5-year survivals of the patients between 60–69 in our series), and of figure 2 (which gives the 5-year survival of the 281 patients of our series who fell in the first group), it can be seen that from the point of view of 5-year survival there is little difference between those patients receiving endocrine treatment and those receiving radical prostatectomy. However, a careful study of the 5 year figures in the radical prostatectomy series shows that those living at the end of the 5 year period are apparent cures. This is not true of the groups treated

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Read at annual meeting, South Central Section, American Urological Association, Tulsa, Okla., September 27, 1950.

by endocrine therapy and it can be expected, therefore, that their curve will rise more rapidly than that of the prostatectomy cases. I believe that this will be particularly true in the younger group of patients since the average survival in years does not vary dramatically with the age of the patient. Colston has emphasized, moreover, that the use of endocrine therapy may make possible the performance of radical surgery on a greater number of patients; in other words, increase the number of patients suitable for radical prostatectomy. He also emphasizes that in many cases, even though a cure is not obtained by total prostatectomy, the relief of obstruction is permanent and in that way the survival of these patients is greatly increased.

TABLE 1. *Five year survival of 587 patients with prostatic cancer, percentage survival at 6-month intervals: Nesbit and Baum's series published in the Journal of the American Medical Association August 12, 1950*

	PERCENTAGE SURVIVAL AT 6 MO. INTERVALS										NO ELIGIBLE	PERCENTAGE DEAD NOT DUE TO CARCINOMA
	6 Mo	12 Mo	18 Mo	24 Mo.	30 Mo	36 Mo	42 Mo.	48 Mo	54 Mo	60 Mo		
With and without metastases on admission												
Control	66.6	51.2	38.1	30.6	25.0	21.9	18.5	17.1	15.8	9.1	504	—
Diethylstilbestrol	94.6	80.9	67.0	55.7	47.0	40.0	31.5	21.8	20.0	18.3	115	26
Orchiectomy	88.9	77.2	65.0	58.2	53.7	43.5	38.2	32.7	29.9	26.2	359	28
Dieth. and orch	96.5	86.8	80.6	68.2	66.4	62.9	53.1	50.4	47.0	36.3	113	21
Endocrine therapy, average										26.9		
No metastases on admission												
Control	72.0	54.0	39.0	32.0	25.0	22.0	—	14.0	—	10.0	273	—
Diethylstilbestrol	93.7	88.9	82.6	76.2	63.5	55.6	43.0	33.5	31.0	29.0	63	33
Orchiectomy	90 8	83.7	72.0	65.1	61.3	51.4	45.0	37.7	35.0	31.2	183	22
Dieth. and orch	93.6	84.7	80.8	74.4	71.8	65.4	57.8	53.9	53.9	43.6	78	30
Endocrine therapy, average										34.3		
Metastases on admission												
Control	69.0	47.0	31.0	20.0	14.0	11.0	—	9.0	—	6.0	231	—
Diethylstilbestrol	96.4	71.2	48.0	30.8	25.0	21.2	15.4	13.4	13.4	9.7	52	18
Orchiectomy	87.0	69.9	68.0	50.6	45.5	35.3	31.3	27.3	24.5	21.6	176	13
Dieth. and orch	99.0	91.5	80.0	54.3	54.3	48.6	42.9	40.0	31.5	20.0	35	11
Endocrine therapy, average										17.1		

In summary then, considering the three pieces of evidence: the curves of Nesbit and our series in conservatively treated patients, the results of Colston, Young, Jewett, and Belt, and the curve of average survival related to age, it would seem that in the younger patients, particularly under 70, when the prostatic carcinoma is limited to the gland, total radical prostatectomy must be seriously considered as the method of treatment.

When the neoplasm has extended beyond the prostatic capsule, or has metasta-

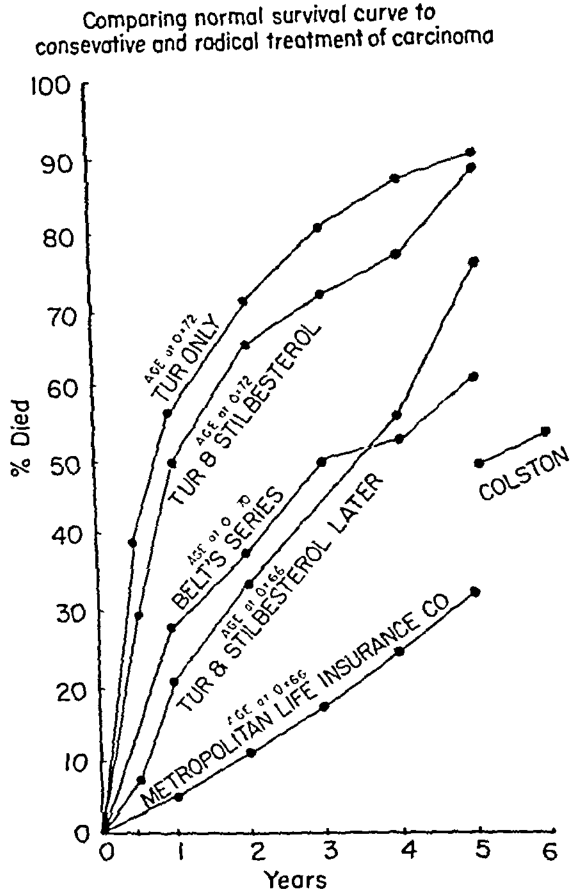

FIG. 1. Illustrating percentage dead at yearly intervals for period of 5 years for several groups of individuals. *a*, Our series that had only transurethral prostatic resection. *b*, Belt's series that had total prostatectomy. c, Our series that had transurethral prostatic resection plus stilbestrol, which was started at time we first saw patient. *d*, Our series that had transurethral prostatic resection, then stilbestrol later when they began to have pain from metastatic involvement. *e*, Colston's series after total prostatectomy. *f*, So-called normal group of 100 individuals whose average age is 66 (Metropolitan Life Insurance statistics).

Note that our total series of cases average 71 years. On the other hand, Colston's and Belt's series average approximately 66 years. If those patients between 60 and 69 in our series are culled out, curve is much lower and much more like that of Belt's. See table 2.

TABLE 2. *The 5-year mortality of those patients in our series between the age of 60 and 69 when first diagnosed*

TREATMENT	PERCENTAGE DEAD AT YEARLY INTERVALS				
	1 year	2 years	3 years	4 years	5 years
TUR only	36.5	58.0	70.9	82.7	87.0
TUR with stilbestrol later	3.4	10.3	20.6	34.4	48.2
TUR and stilbestrol	24.6	40.2	62.3	66.2	68.8

sized, radical surgery with the idea of cure is no longer to be considered. The problems now are: 1) the relief of bladder neck obstruction; 2) endocrine control of the neoplasm.

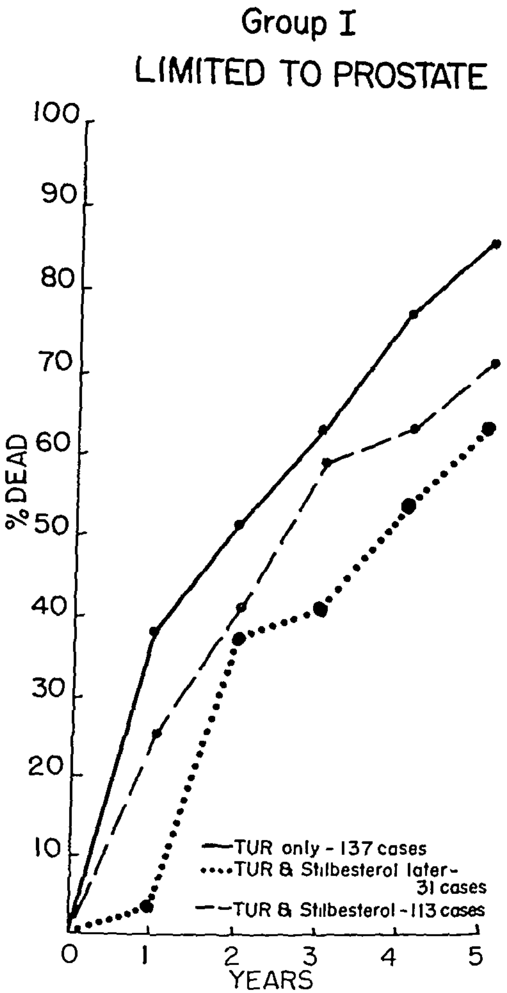

FIG. 2. Showing 5-year survival of our group 1 cases. These are patients who, when first seen, had carcinoma as far as one could ascertain, limited to prostate with no definite local extension and no definite metastasis. *a*, Showing 137 patients in this group who had no endocrine therapy and who had transurethral prostatic resection for relief of obstruction. *b*, Showing 113 patients who had transurethral prostatic resection and endocrine therapy as soon as we saw them. *c*, Showing 31 patients in this group who had stilbestrol only when they began to have pain.

The relief of bladder neck obstruction may be accomplished in one of four ways: 1) transurethral resection; 2) suprapubic cystostomy; 3) reaction to hormones; 4) radical prostatectomy.

In this series, transurethral resection was used in practically every case for relief of bladder neck obstruction. There was no evidence that it brought about an increased growth of the neoplasm. However, that question has been raised in those cases where much bladder irritation and evidences of poor healing occur after the transurethral resection. Such cases are relatively uncommon and in such instances suprapubic cystostomy should be performed instead of further resection. Suprapubic cystostomy without resection has not been done frequently enough in our series to make it possible to demonstrate that the trauma to the neoplasm, incident to the resection, is or is not of significance. It would be of interest to study the 5-year survival of such a series.

In an occasional instance radical prostatectomy for relief of the symptoms and signs of obstruction may offer more than the above two methods (Colston).

Many observers have noted that a large percentage of patients have had their obstruction relieved by endocrine treatment alone. This has not been our experience in a significant number of cases.

In summary then, in our series, transurethral resection and suprapubic cystostomy were the procedures of choice and necessity for the relief of the bladder neck obstruction. Endocrine control was ineffectual for this purpose.

TABLE 3. *Number of cases surviving at yearly intervals*

TREATMENT	UNDER 1 YEAR	1 YEAR	2 YRS.	3 YRS.	4 YRS.	5 YRS.	6 YRS.	7 YRS.	8 YRS.	9 YRS.	OVER 10 YRS.	TOTAL
TUR only	135	56	47	34	22	10	6	6	12	3	4	335
TUR with stilbestrol later	6	11	10	8	10	16	3	8	1	2	4	79
TUR with x-ray	20	12	6	1	1	—	—	2	—	—	—	42
Palliative x-ray only	9	4	3	1	—	—	—	2	—	1	—	20
Stilbestrol first	14	18	6	7	6	7	3	3	—	—	—	64
TUR + stilbestrol	74	50	45	15	13	31	18	9	—	—	1	256
Not treated at S. U. I.	39	8	3	1	2	—	—	—	—	—	—	53
Miscellaneous	3	1	1	—	—	—	—	—	—	—	—	5
Totals	300	160	121	67	54	64	30	30	13	6	9	854

Endocrine control of the neoplasm: The endocrine therapy of carcinoma of the prostate, which has been used extensively since the 1941 reports of Huggins and Munger, has revolutionized that status of those patients with carcinoma of the prostate which is not amenable to complete removal, and has altered tremendously the thinking with regard to the control of this neoplasm. There is no question that in the vast majority of patients such therapy yields dramatic improvement: relief from pain, decrease in size of the original tumor and its metastases, and general improvement. This gratifying result, however, with the exception of the relief of pain, which may be lasting, is only temporary and its duration varies from a few months to several years. The exact place of endocrine treatment in the management of these patients is still a very moot one, and as one gathers more experience one's ideas of the fundamental factors concerned change. There is no question that carcinoma of the prostate responds in some way to alteration in the endocrine balance, but the fundamental facts involved in this are unknown.

It was assumed originally that if the androgen influence could be completely eliminated or "neutralized," that carcinoma of the prostate could be "stabilized." It is upon this basis that our series of cases were treated. The results of this treatment in 399 out of our 854 cases compared with the results in the remaining 455 cases which did not have endocrine therapy is illustrated in tables 3 and 4 and figures 4 and 5. These may be compared with the results in Nesbit and Baum's series which are shown in table 1. It is extremely important in charting these results to compare them with the figures for the average survival in groups of the same age. Figure 6 gives these for the ages 65, 66, 70, and 72. These are the age groups of importance in this discussion. Note carefully how

TABLE 4.

TREATMENT	TOTAL CASES	# OF 5 YR SURV.	% OF 5 YR. SURV.	% WITH LATER TREATMENT	AVG SURV.	AVG AGE
TUR only	335	41	12.2	20.6	2.22	72 1
TUR with stilbestrol later	79	34	43	44.4	4.52	70.5
TUR and immediate x-ray	42	1	2.4	14.3	1.26	67.8
TUR, x-ray, stilbestrol later	2	0	0	0	2.48	61.5
Palliative x-ray	20	3	15.0	15	2 17	65.5
Stilbestrol first	64	13	20.0	(TUR) 34.4	2.69	69.9
TUR, stilbestrol initially	256	59	23.0	11.3	2.63	72 5
No treatment at S. U. I.	53	0	0	1 (S-P)	—	—
X-ray and later stilbestrol	3	0	0	0	2.50	—
Total Cases	854	151	17.68	19.67	2.54	

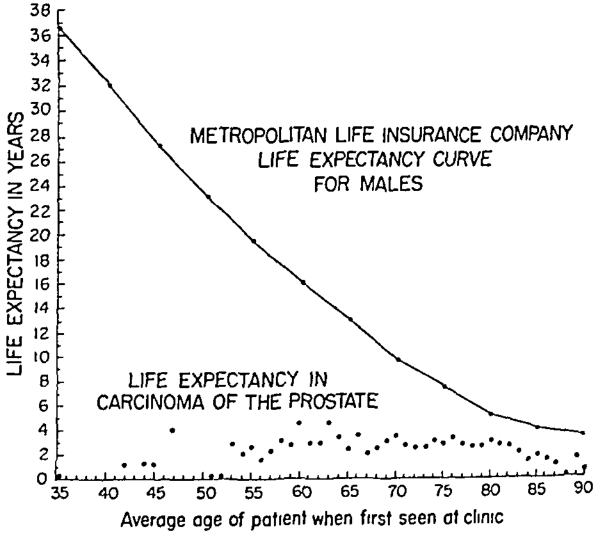

FIG. 3. Comparing Metropolitan Life Insurance life expectancy curve for males with survival of patients in our total series. Showing average survival of our whole group of 854 patients with carcinoma of prostate. Notice that average survival runs in neighborhood of 2 to 3 years. It seems to be relatively independent of age of patient except that possibly highest survival is in period between 60 and 70 years.

the slopes of the curves vary with age. This is exaggerated in the upper age groups.

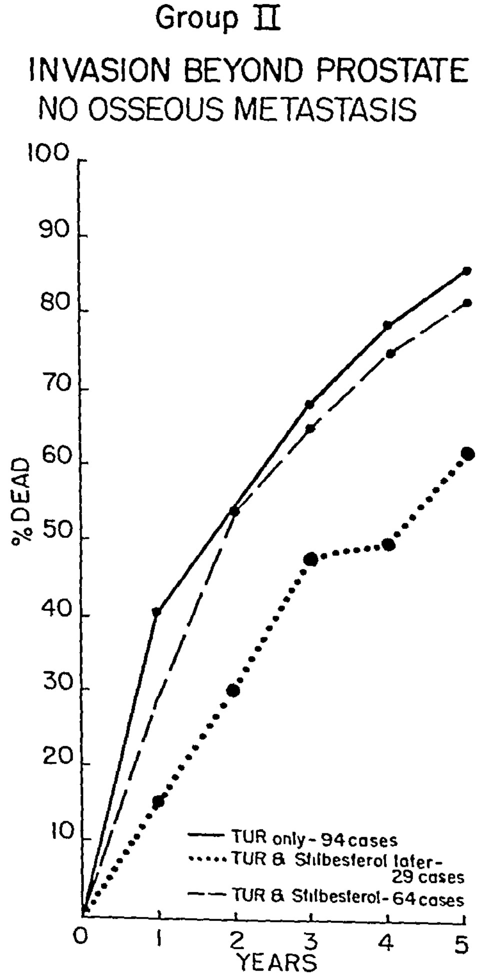

FIG. 4. Illustrating percentage dead for first 5 years in those patients in whom at time of admission, carcinoma definitely extended beyond the prostate, but no definite metastases were present. Ninety-four patients did not receive endocrine therapy, 64 patients received endocrine therapy as soon as they were seen, and 29 patients who did not receive endocrine therapy until they began to have pain.

From these figures it would seem:

1) That the combined influence of orchiectomy and stilbestrol is superior to that of stilbestrol alone. In reviewing our material and comparing it with Nesbit's report, this seems a quite definite conclusion.

2) There is also some indication that in those cases where stilbestrol was not given until later, the percentage survival was increased. The total number of cases in this group is relatively small and I am frankly not sure how to evaluate

these results. The very careful and comprehensive study of Rusche presented before the North Central Section of the American Urological Association on October 7, 1949, covering a series of 765 patients who had endocrine treatment comes to a very different conclusion. He states "there is no evidence to support any preference as to early or late orchiectomy."

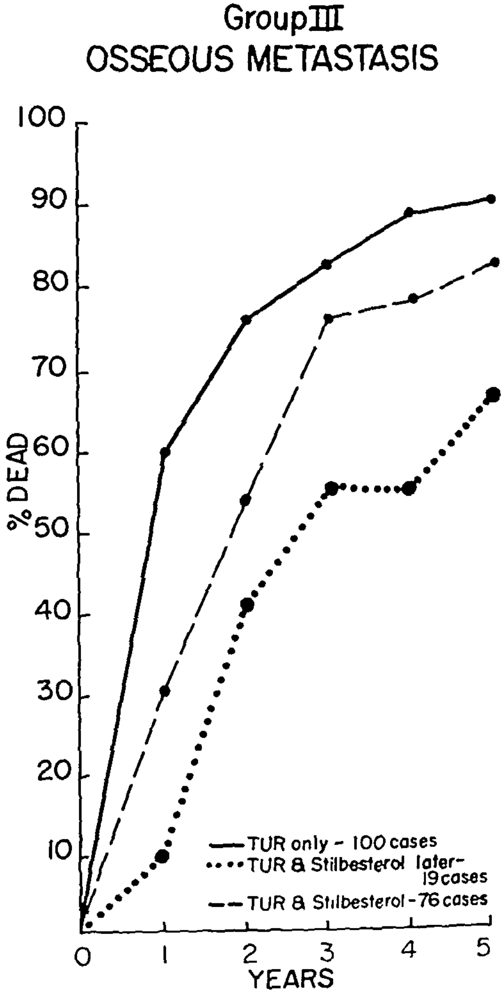

FIG. 5. Illustrating group that had metastases at time of admission and showing percentage dead for each year for the first 5 years after they were seen. One hundred patients did not receive endocrine therapy, 19 patients received endocrine therapy only when they began to have pain, and 76 patients received endocrine therapy at time they were first seen. Compare survival in this group with groups that did not have metastases and with group that had no extension beyond prostate. Longer the survival, smaller the tumor, but general trend of curves is same.

The dosage of diethylstilbestrol used in these cases was 1 to 5 mg. daily. In cases treated later, it has been frequently demonstrated that when small doses failed to produce results, much larger doses sometimes as high as a thousand milligrams per day did produce relief from pain and allowed the patient to return to his normal activities.

This brings us back to the question of the fundamental factors involved in this type of therapy of carcinoma of the prostate. Is it actually an androgen-estrogen imbalance or a steroid imbalance? Just what part do the adrenals and the pituitary play? Should x-ray treatment to the adrenals as advised by Munger or x-ray treatment to the pituitary as performed in some cases by Alyea be part of the routine treatment? Should x-ray treatment be given to the local lesion in addition to castration and estrogenic therapy as suggested by Rusche? What factors should be followed to tell us whether a patient's carcinoma is stabilized or not? Is it pain? Is it change in the character of the neoplasm? Is it urinary estrogen? Is it the urinary ketosteroids? Is it the urinary gonadotrophin? Is it

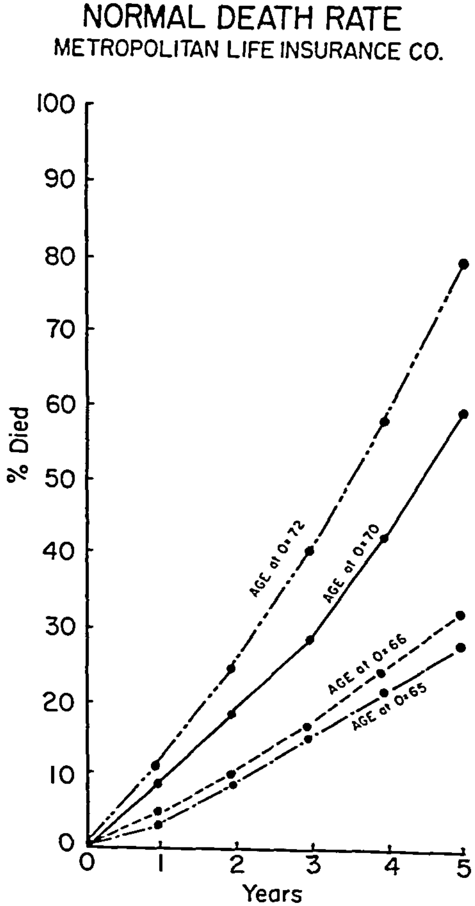

FIG. 6. Showing 5-year survival of group of average individuals of 65, 66, 70 and 72 years of age. These are charted in exactly same manner as our patients. They show difference in slope of curves depending upon age of individuals.

blood acid and alkaline phosphatase activity? Are steroids other than the androgens or estrogens involved, etc.?

One of the first reports indicating that the endocrine control of carcinoma of the prostate was not simply a question of neutralization of androgen by estrogen was the report of Brendler. He reported testosterone therapy of three patients with prostatic cancer with clinical improvement. The more recent report of Trunnel and Duffy on the influence of certain steroids on the behavior of human prostatic cancer is even of more interest. They treated 15 patients with progesterone in doses of 25 to 300 mg. daily. Thirteen of these fifteen patients responded favorably to progesterone administration; seven of these previously had a spontaneous relapse after castration or estrogen therapy. In treating some of these patients with pregneninolone they found evidence of pluripotential response. Several patients improved dramatically on 25 to 100 mg. of the substance a day, whereas other patients receiving similar doses grew rapidly worse with rises in the serum acid and alkaline phosphatase accompanying clinical deterioration. There seems little doubt that pregneninolone had a variable effect on prostatic cancer.

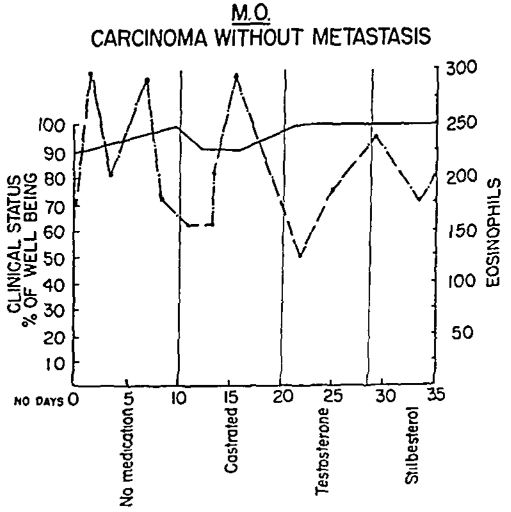

Fig. 7

A similar dual effect was observed by these observers in one patient receiving progesterone. This patient had been well controlled with 200 mg. intramuscularly in oil, but when a total of 1500 mg. was given subcutaneously in pellets he became rapidly worse. In our own experience we have not observed any evidence of pain and elevation of acid phosphatase following the administration of very large doses of estrogens; however, Scott, and Trunnel and Duffy have noticed a few cases where this has occurred. From these experiences and our own experiences it seems that the older concept of androgen neutralizes estrogen does not completely explain the phenomena which have been observed. With regard to the above the following three clinical observations are of interest.

First is that of M. O., aged 66, whose chart is illustrated in figure 7. He had a histologically proven carcinoma of the prostate. He felt well, his only symptoms were those of prostatic obstruction which had been overcome by means

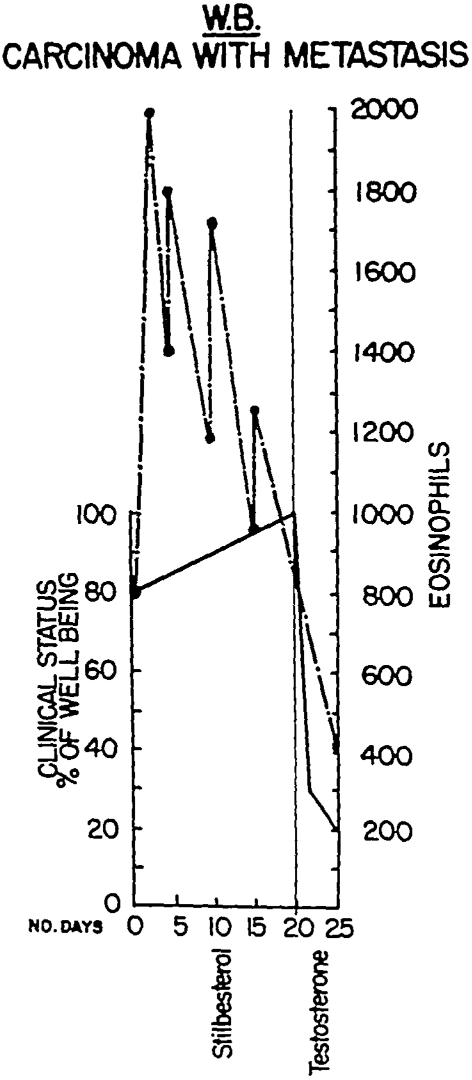

FIG. 8

of an indwelling urethral catheter. The chart shows that we considered him 90 per cent of normal as far as his general well-being was concerned. Eosinophil counts were made to see if there was any stimulation of the adrenal as a result of stress associated with his neoplasm. These were within normal range. On the tenth day a bilateral orchiectomy was carried out. He continued to feel fine, but for the first few days following the operation, the eosinophil count came down because of stimulation of the adrenal associated with the operative procedure. It then went back to the original values. On the twentieth day, ten days after the castration, he was given 100 mg. testosterone propionate intramuscularly daily. There was some lowering of the eosinophil count but not markedly so. He continued to feel fine and he did not realize that we were giving him anything more than saline intramuscularly. Ten days later, 20 days after the castration, he was placed on stilbestrol therapy and again there was no objective change during the period that he was followed, either in the tumor itself or subjectively.

Contrast this with the figure 8 of patient W. B., aged 73. He had carcinoma of the prostate with metastases, and was feeling good when he entered the hospital. His only complaint was that of bladder neck obstruction which was overcome with an indwelling catheter. He was given 100 mg. stilbestrol daily during the first 20 days in the hospital. He had been on stilbestrol prior to admission to the hospital. His eosinophil count was high, higher than that usually seen in normal individuals. The cause of this I do not know. On the twentieth day and for the next 5 days, testosterone propionate, 100 mg. intramuscularly was given. Within 24 hours he had a great deal of pain and at the same time showed marked clinical deterioration. The eosinophil count went down rapidly from a previous count of 1200 to 800 and two or three days later was down to 400. It jumped back and he improved when the testosterone was discontinued and the stilbestrol re-instituted.

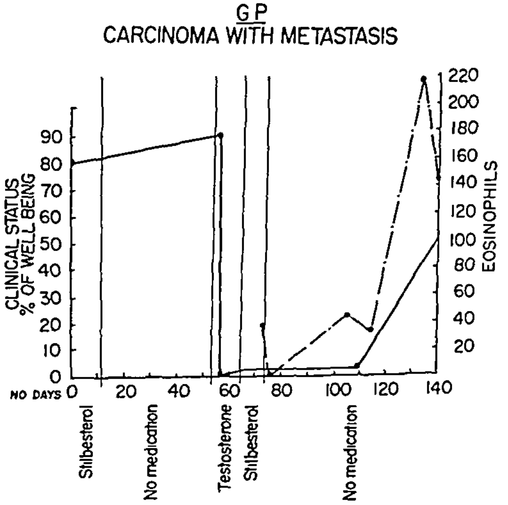

FIG. 9

Another patient who is of interest in this respect is illustrated in figures 9 and 10. G. P., aged 60, is a patient who had had an orchiectomy 1 year prior to this admission to the hospital. He entered the hospital urinating quite satisfactorily but having pain due to bony metastases. Large doses of stilbestrol (500 mg. daily) produced subjective improvement. Medication was discontinued and for 35 days no medication was given. During this period he continued to feel well. He was then given two doses of 25 mg. testosterone propionate intramuscularly. There was tremendous clinical deterioration, pain returned and it appeared that he was going to die. The testosterone was discontinued and he was placed on large doses of stilbestrol (300 mg. daily). He improved somewhat but had to be given supportive and parental therapy. During the recuperative period the first eosinophil count was carried out. It was very low and remained very low for the following 30 days. It then steadily improved, going back up to normal and during this period of improvement in the eosinophil count he subjectively and objectively improved tremendously, even though he was on no medication. Following this rise in eosinophil count and clinical improvement the patient was given ACTH, 25 mg. every 6 hours for 8 doses. The patient was observed hourly. The clinical status improved after 8 hours. The eosinophil count gradually decreased showing adrenal cortical stimulation. This would seem to indicate that in a patient whose carcinoma is known to be sensitive to testosterone propionate adrenal cortical stimulation by ACTH did not produce a substance which acted upon the carcinoma like testosterone propionate had.

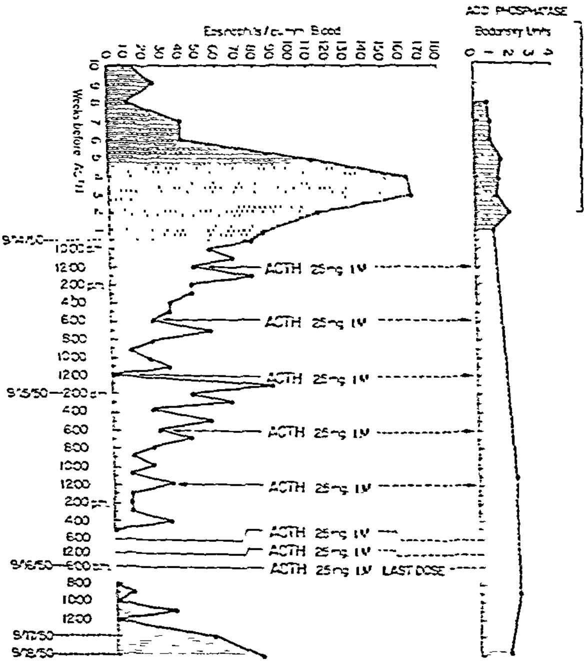

FIG. 10

The explanation of the phenomena described above is not yet at hand. Is the deterioration of the patient's condition which occurs in some cases where testosterone is given associated with the production of increased adrenal activity which in turn produces an eosinopenia? Is the eosinopenia a purely coincidental phenomenon? Why do not all patients react in a similar manner? Is it possible to tell beforehand who will or will not react in a detrimental manner to testosterone? What is the underlying reason for the variation in reaction of the carcinoma of the prostate to such substances as progesterone and pregneninolone?

Rusche's findings that those patients who received regional x-ray therapy plus endocrine treatment did better than those with endocrine treatment alone, may indicate that such radiation made the tumor cells more responsive to hormonal treatment. It also would be of interest to know whether or not x-ray treatment to the pituitary or adrenal would prevent a deterioration seen with testosterone.

SUMMARY

An analysis of a series of 854 patients with carcinoma of the prostate followed for 5 years or more, a partial review of the literature and a study of individual patients given unusual types of treatment would suggest the following outline for the treatment of patients with carcinoma of the prostate:

1) In those patients in whom the carcinoma is limited to the prostate, total prostatectomy should be considered in those under the age of 70.

2) Where the lesion has extended beyond the prostate and become inoperable, the problems are relief of bladder neck obstruction and endocrine control of the neoplasm. In our series the procedures of choice and necessity for relief of the bladder neck obstruction were transurethral resection and suprapubic cystostomy.

3) Endocrine control of the neoplasm presents many fascinating and unsolved problems. The results of this study would seem to indicate:

a) That castration should be part of endocrine control in the majority of cases.

b) That stilbestrol therapy should be reserved for later treatment when the patient begins to have evidences of pain and other deteriorating changes rather than when he is first seen. In other words, it should be reserved for the relapse. A satisfactory dosage may vary from 1 mg. to 1000 mg. a day.

c) There was no evidence of a difference in response to stilbestrol therapy based upon the presence or absence of metastasis or the histological grade of the neoplasm.

d) That endocrine control of carcinoma of the prostate is not simply a question of neutralization of androgen by estrogen. Variations in response to the administration of testosterone in several patients are reported here. It is of interest that in those cases where clinical deterioration occurred as a result of testosterone administration, eosinopenia occurred. The explanation of this phenomenon is not known. However, it may be very well an evidence of extreme adrenal stimulation. The question raised is, whether or not the eosinophil count can be used as one of the indices of activity of the tumor in much the same way as the serum acid phosphatase activity can be used in some cases.

REFERENCES

Belt, E.: Radical perineal prostectomy in early carcinoma of the prostate. J. Urol., 48: 287–297, 1942.

Brendler, H., Chase, W. E. and Scott, W. W.: Prostatic cancer: Further investigation of hormonal relationships. Arch. Surg., 61: 433–440, 1950.

Colston, J. A. C.: Surgical removal of cancer of the prostate gland, the radical operation. J.A.M.A., **127:** 69–74, 1945.

Herbst, W. P.: Effects of estradiol dipropionate and diethylstilbesterol on malignant prostatic tissue. Tr. Am. A. Genito-Urin. Surgeons. **34:** 195–202, 1941.

Huggins, C. and Hodges, C. V.: Studies on prostatic cancer. I. The effect of castration, of estrogen and of androgen injection on serum phosphatases in metastatic carcinoma of the prostate. J. Cancer Res., **1:** 293–297, 1941.

——, Stevens, R. R. and Hodges, C. V.: Studies on prostatic cancer. II. The effects of castration on advanced carcinoma of the prostate gland. Arch. Surg., **43:** 209–223, 1941.

——, Scott, W. W. and Hodges, C. V.: Studies on prostatic cancer. III. The effects of fever, of desoxycorticosterone and of estrogen on clinical patients with metastatic carcinoma of the prostate. J. Urol., **46:** 997–1005, 1941.

Huggins, C. and Hodges, C. V.: Bilateral adrenalectomy in prostatic cancer. Ann. Surg., **122:** 1031–1041, 1945.

Jewett, H. J.: Radical perineal prostatectomy for cancer of the prostate: An analysis of 190 cases. J. Urol., **61:** 277–280, 1949.

Munger, A. D.: Experiences in the treatment of carcinoma of the prostate with irradiation of the testicles. J. Urol., **46:** 1007, 1941.

Nesbit, R. M. and Plumb, R. T.: Treatment of prostatic carcinoma by castration and by administration of estrogenic hormone. Univ. Hosp. Bull., Ann Arbor, **12:** 14–15, 1946.

——, and Baum, W. C.: Endocrine control of prostatic carcinoma. J.A.M.A. **143:** 1317–1320, 1950.

——, Cancer of the prostate: General considerations. Dallas M. J. **33:** 81–84, 1947.

Scott, W. W. and Vermeulen, C.: Studies on prostatic cancer; excretion of 17-ketosteroids, estrogens and gonadotropins before and after castration. J. Clin. Endocrinol., **2:** 450–456, 1942.

Trunnell, J. B., and Duffy, B. J.: The influence of certain steroids on the behavior of human prostatic cancer. Tr. N. Y. Acad. Sc. Series II, **12:** 238–241, 1950.

Young, H. H.: The cure of cancer of the prostate by radical perineal prostatectomy (prostato-seminal vesiculectomy): history, literature and statistics of Young's operation. J. Urol. **53:** 188–256, 1945.

to tell beforehand who will or will not react in a detrimental manner to testosterone? What is the underlying reason for the variation in reaction of the carcinoma of the prostate to such substances as progesterone and pregneninolone?

Rusche's findings that those patients who received regional x-ray therapy plus endocrine treatment did better than those with endocrine treatment alone, may indicate that such radiation made the tumor cells more responsive to hormonal treatment. It also would be of interest to know whether or not x-ray treatment to the pituitary or adrenal would prevent a deterioration seen with testosterone.

SUMMARY

An analysis of a series of 854 patients with carcinoma of the prostate followed for 5 years or more, a partial review of the literature and a study of individual patients given unusual types of treatment would suggest the following outline for the treatment of patients with carcinoma of the prostate:

1) In those patients in whom the carcinoma is limited to the prostate, total prostatectomy should be considered in those under the age of 70.

2) Where the lesion has extended beyond the prostate and become inoperable, the problems are relief of bladder neck obstruction and endocrine control of the neoplasm. In our series the procedures of choice and necessity for relief of the bladder neck obstruction were transurethral resection and suprapubic cystostomy.

3) Endocrine control of the neoplasm presents many fascinating and unsolved problems. The results of this study would seem to indicate:

a) That castration should be part of endocrine control in the majority of cases.

b) That stilbestrol therapy should be reserved for later treatment when the patient begins to have evidences of pain and other deteriorating changes rather than when he is first seen. In other words, it should be reserved for the relapse. A satisfactory dosage may vary from 1 mg. to 1000 mg. a day.

c) There was no evidence of a difference in response to stilbestrol therapy based upon the presence or absence of metastasis or the histological grade of the neoplasm.

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REFERENCES

Belt, E.: Radical perineal prostectomy in early carcinoma of the prostate. J. Urol., 48: 287–297, 1942.

Brendler, H., Chase, W. E. and Scott, W. W.: Prostatic cancer: Further investigation of hormonal relationships. Arch. Surg., 61: 433–440, 1950.

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NEEDLE BIOPSY OF THE PROSTATE: A NEW NEEDLE BIOPSY INSTRUMENT

W. F. MELICK

From the Department of Urology, St. Louis University School of Medicine, St. Louis, Mo.

The chief difficulty in the treatment of prostatic carcinoma seems to be its early recognition. The typical late case with a fixed, hard, irregular prostatic gland offers no diagnostic problem, but it is also beyond the hope of cure by any available treatment.

It is becoming more evident, by the growing list of reported cures, that early prostatic carcinoma can be successfully eradicated by radical removal, either by the retropubic or perineal route. Unless careful rectal examinations are made by all physicians who do routine physical examinations on male patients, it is true that one cannot hope to increase his percentage of prostatic carcinoma cases in which the patients are seen early enough for hope of cure through radical surgery.

One cannot deny, of course, that when a suspicous induration is present, a biopsy should be obtained. It is also common knowledge, however, that the vast majority of urologists do not practice routine open perineal biopsy. Perineal exposure and frozen section biopsy do have two rather major disadvantages as routine procedures. First, and of decidedly less importance, if the report is benign, one hesitates to procede with a routine perineal enucleation because of the higher incidence of incontinence and prolonged hospitalization. Secondly, and more serious, is the inability of the surgeon and pathologist to decide in every case from the frozen section alone whether or not the tissue is carcinoma.

A needle biopsy permits microscopic examination of routinely fixed and stained slides with a more positive diagnosis. It is also a simple procedure which later permits any type of prostatic surgery which the operator may select. One great disadvantage exists, which is if the exact nodule is not biopsied, one may miss a carcinoma. Having tried most, if not all, of the existing needles with indifferent success, the following needle was devised.

The outer sheath (fig. 1) contains a trocar point and a fenestra with a sharp edge as in the cold punch type of resectoscope. The inner sheath (fig. 1) carries a replaceable cutting blade, which permits ready replacement with a sharp knife at all times. When closed, the knife blade occludes the fenestra (fig. 1), and the position of the fenestra is marked by a knob on the collar of the outer sheath (fig. 1).

General anesthesia has been used because the better relaxation permits careful palpation and accurate removal of small suspicious nodules. The patient is placed in lithotomy position and prepared and draped. One finger is inserted into the rectum, the nodule identified, and a stab wound made through the skin just above the anus on the side of the nodule. The assembled needle is then carefully inserted between the rectum and prostate. When the needle is judged

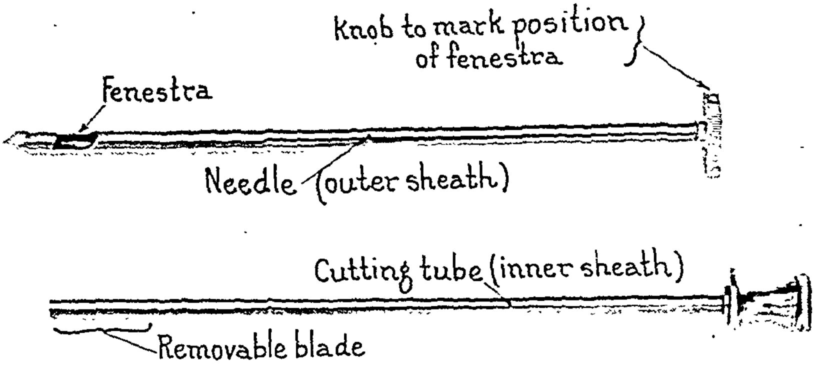
Knob to mark position of fenestra
Fenestra
Needle (outer sheath)
Cutting tube (inner sheath)
Removable blade

FIG. 1

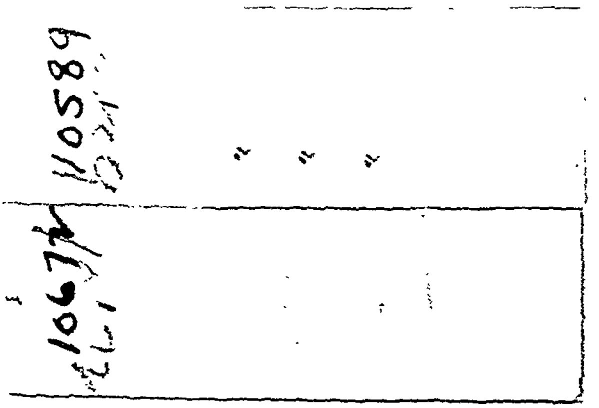

FIG. 2. Photograph of stained, fixed, and mounted microscopic slide of two different cases, showing amount of tissue available for microscopic examination.

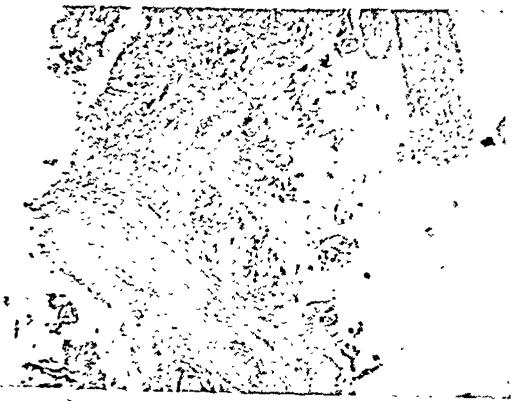

FIG. 3. Photomicrograph of tissue shown in figure 2 showing clearly carcinoma with perineural involvement.

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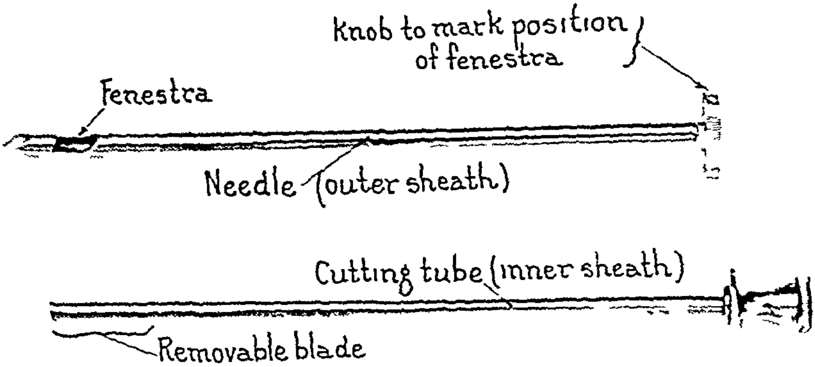
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Fenestra
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FIG 1

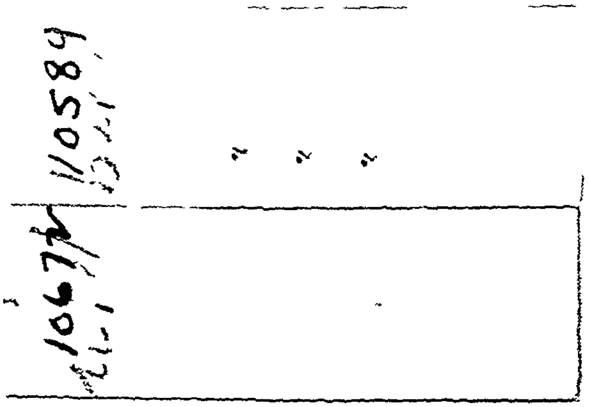

FIG 2 Photograph of stained, fixed, and mounted microscopic slide of two different cases, showing amount of tissue available for microscopic examination

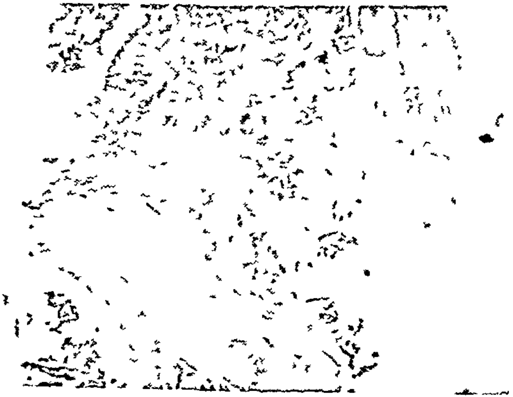

FIG 3 Photomicrograph of tissue shown in figure 2 showing clearly carcinoma with perineural involvement

to be in proper position, the obturator is withdrawn so that the fenestra can be palpated. If it is under the nodule, the needle is rotated 180 degrees, and the nodule engaged, using the rectal finger as a fulcrum. The knife is then pushed forward with a rotary motion and the needle withdrawn. Because of the more than adequate size of the specimen, brisk bleeding is sometimes encountered on withdrawal, but this has always been easy to control with simple perineal pressure for a few minutes. In several instances of younger individuals with small fibrotic prostates, the bladder has been inadvertantly punctured and urine has run out of the needle. No untoward reactions have been seen in such cases. Figure 2 shows a typical specimen removed by the needle which proved to be carcinoma of the prostate on section. Figure 3 shows the microscopic appearance; the diagnosis is made certain by the appearance of perineural invasion.

The following 4 cases are reported briefly to illustrate the value of the needle biopsy.

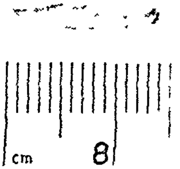

FIG. 4. Gross specimen removed by needle biopsy instrument

CASE ABSTRACTS

G. H., a 65 year old white man, stated that he had been examined by another urologist who told him that he had prostatic calculi. Rectal examination disclosed a suspicious nodule in the right half of the posterior lobe. He had had no backache and no weight loss. Cystoscopy and metastatic x-ray series were negative for invasion or metastases. Blood alkaline and acid phosphatase determinations were normal. Needle biopsy (figs. 2 and 3) was positive for carcinoma. Radical retropubic prostatectomy was carried out and operable carcinoma found.

J. W., a 67 year old white man, had a suspicious prostate. Cystoscopy showed no fixation. Metastatic x-ray series were negative for metastases. He had had no weight loss or backache. Blood alkaline and acid phosphatase were normal. Needle biopsy was reported as carcinoma. Radical retropubic prostatectomy was performed.

C. B., a 60 year old white man, was seen for routine examination. A suspicious nodule was palpable. Needle biopsy was positive for carcinoma. Metastatic x-ray series were negative for metastases. He had no symptoms. Blood alkaline and acid phosphatase determinations were normal. Radical perineal prostatectomy was done.

N. W., a 78 year old white man, was seen because of back pain without demonstrable metastases on x-ray. He had no other symptoms and blood alkaline and acid phosphatase determinations were normal. The prostate was small, not fixed, but of suspicious consistency. Needle biopsy showed carcinoma.

Because of the patient's age and severe back pain, radical removal was not done; his symptoms are being relieved on stilbesterol.

DISCUSSION

Some experience is necessary to get adequate pieces of prostate with the described needle. In my first cases I frequently did not get prostatic tissue, or I am sure, at least did not get it from the suspected area of the gland. With practice my percentage of needle biopsies has shown a marked rise on the number of carcinomas found. I cannot emphasize too strongly that while a positive needle biopsy permits early radical surgery, a negative biopsy certainly does not rule out carcinoma. This is the inherent defect in all needle biopsy procedures. In such cases of negative needle biopsy, the only safe and sensible course is to do perineal exposure and biopsy. It might also be mentioned that in the cases who had needle biopsy and later subjected to radical surgery no difficulty was encountered at the site of the biopsy. Although bleeding in several cases was profuse from the stab wound in the skin, no evidence of reaction could be found at the time of surgery.

SUMMARY

A new needle for perineal prostatic biopsy has been presented.

The pieces of tissue secured have been adequate to prove the clinical suspicion of early prostatic carcinoma in many cases.

Like all needle biopsy procedures, if the biopsy is negative, it does not necessarily rule out carcinoma.

I wish to express my appreciation to the American Cystoscope Makers, Inc. who made the needle for me.

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OSTEITIS PUBIS

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Beer who first recorded in the English language (1924) the condition now referred to as osteitis pubis, stated: "During the last dozen years following suprapubic operations on the bladder we have repeatedly observed a curious and painful complication of periostitis" and again, "It is surely a rare complication although we have seen every year one or more cases during the past twelve years."

I have believed for some time that this complication of lower urinary tract surgery is far more common than one would be led to believe by the literature. My reason for presenting this paper to you today is to record a large series of cases presenting this distressing complication. As a result of a questionnaire addressed to my urological colleagues in Australia and New Zealand, some forty-four cases have been collected from the practices of 16 out of 37 urologists who answered the questionnaire. Of these, 7 cases occurred in my own practice.

Prior to 1947, practically all cases were reported as occurring after the second stage of a two-stage suprapubic prostatectomy. Since that date the cases presenting this complication have become more protean in their nature. In the cases here recorded, 5 occurred after cystectomy either partial or total, 29 after retropubic prostatectomy, 5 after suprapubic prostatectomy, 3 after transurethral prostatectomy, 1 after external urethrotomy and 1 after rupture of the posterior urethra, both these last 2 cases in association with suprapubic cystotomy (table 1).

Perhaps the main interest lies in the occurrence of osteitis pubis after the use of the retropubic route of approach to the prostate as elaborated in recent years by Terence Millin. Though comparatively rare in the experience of the originator of the operation, his latest statistics being 9 cases in 1,100 retropubic prostatectomies, its incidence in a high percentage of prostatectomies performed by this route has led various urologists to view the procedure with concern and in some instances to abandon it. Moore reports 8 cases occurring in the first 65 prostatectomies done by this method and in the cases here presented it is noted that 65 per cent followed on this operation, one urologist reporting the occurrence of 7 cases of osteitis pubis following on 200 cases of retropubic prostatectomy. In this series, apart from one case diagnosed in 1934, no case was seen prior to 1944.

The clinical picture may be mild or severe, symptoms beginning from 4 to 28 days after the relative operation. The onset may be delayed for upwards of 4 months as in 1 case in this series. The severe cases appear to predominate in numbers.

The clinical and radiological features of the disease have been adequately dealt with in previous reports. To summarize however, pain is the outstanding

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symptom beginning in the midline and associated with great tenderness on pressure over the symphyseal region. With extension to the rami of the pubes, pain is complained of in the inguinal regions, on both sides and the upper medial aspect of the thigh. Later the ischia become involved with pain in the perineum and the buttocks. The muscles attached to the affected bones become spasmodic, any movement of the pelvis causing contractions which are excruciatingly painful. Micturition becomes painful particularly at the end of the act and because of the contraction of the levatores ani muscles and the use of the bed-pan, defecation becomes a misery. The most obvious spasm is that of the adductor muscles and the patient lies in bed in gross fear of any movement. This is a pathognomic picture hardly comparable with that seen with any other condition in the body. The dramatic symptom complex may persist for many weeks or some months, and in practically all cases little alleviation is produced by any therapeutic measure. With the passage of the hyperacute stage the act of walking or sitting may be painful as long as 12 months. In the milder cases the symptoms are far less severe and their duration shorter.

TABLE 1

	Cases
Cystectomy, partial or complete	5 cases
Retropubic prostatectomy	29 cases
Suprapubic prostatectomy	5 cases
Transurethral prostatectomy	3 cases
External urethrotomy	1 case
Rupture of the prostatic urethra	1 case
	44 cases

The earliest radiological changes may be seen about the third week. They occur in the symphysis pubis where a motheaten appearance of the cartilage and the adjacent portions of the pubes may be seen. The brunt of the disease at this stage affects this joint, the cartilage disappearing and the pubic bones being splayed out up to 1.5 cm. With the progress of the disease areas of rarefaction are seen in both rami of the pubes on each side and in the severe cases similar changes are noted in the ischia. Evidence of lifting and fraying of the periosteum is seen particularly in relationship to the muscular attachments. With retrogression recalcification takes place, even though symptoms may be still present, and after a period of months complete bony restitution will occur. In the symphyseal region bony ankylosis ensues, while in the region of their attachments large masses of bone will extend into the muscles particularly the adductor group. No sequestrae have been reported. Abscess formation has been noted on occasion, but each of the recorded collections of pus has been very small, 5–10 cm. No abscess formation occurred in these 44 cases.

No treatment offers any certainty of either cure or amelioration of the symptoms. In the cases here recorded some relief of symptoms was obtained by chemotherapy in two cases, and in one rapid relief followed the exhibition of vitamin B. In all the other cases the routine measures of chemotherapy, vitamin therapy, radiotherapy, diathermy and radiant heat were tried without significant result.

ETIOLOGY AND PATHOLOGY

The greatest interest of osteitis pubis lies in its pathological nature and the relationship of this to its etiology. Various features of this unusual disease require adequate explanation.

1) Osteitis follows on operations involving the opening of the bladder. Exceptions are recorded as following transurethral resection. In the two cases mentioned by Bruskewitz and Ewell, both gave a history of severe bleeding in the anterior region of the bladder neck requiring an excessive degree of coagulation for hemostasis. In a female these observers record a further unusual case following on the removal of a stone from the lower end of the ureter. In this present series all 3 of the cases of transurethral resection which were followed by osteitis pubis required cystotomy in their aftercare, because of hemorrhage, extravasation or perivesical abscess respectively. That the condition is related to the opening of the prevesical space is strongly suggested by the great number of cases following on retropubic prostatectomy. It is difficult to reconcile this with the earlier occurrence of the complication after the second stage of a two-stage supropubic prostatectomy. One would expect that the prevesical space would be sealed off after the preliminary cystotomy and that with a correctly placed abdominal incision and a tube inserted into the highest point of the bladder that there would be little chance in the second stage, of trauma to the pubes or opening up of the prevesical space.

An odd case has been reported where there was no drainage of urine involved, such as the case after confinement, of Soderlund (cited by Wilensky), and that on a similar basis mentioned by Millin, but available details are insufficient for comment to be made.

2) Osteitis pubis is a comparatively new disease. Twenty-six cases had been recorded in the literature up to 1941, twelve of them by Edwin Beer. That the condition could have passed unobserved prior to this is most unlikely since most cases follow the severe pattern and the pain and disability are such that radiological investigation would inevitably have been carried out and the obvious changes discovered. My own experience has followed closely on that of most other observers. In consultation with a surgical colleague in 1944, I had seen 1 case following on suprapubic prostatectomy. It was not until January 1948, that I suffered this complication in my own surgical practice and within a month 6 cases had been diagnosed. It is remarkable that many urologists with an experience of thousands of cases of pelvic surgery involving the opening of the bladder have gone through their urological life without seeing one case, while others with similar experience are now confronted with a spate of them. In the search for an explanation for this recent occurrence it was early suggested that the use of chemotherapeutic powders in the wound (a procedure of recent origin) might provide the cause. From a theoretical point of view this could produce rapid healing of the superficial layers of the wound and cause infection to be pent up in the depths. This theory is disproved by the fact that in this series osteitis pubis occurred in 50 per cent of the cases in the practice of surgeons who do not use any powder in their postoperative toilet of wounds.

3) The third factor still unsatisfactorily explained is the delay of onset from 15 days to very much longer periods, the onset being associated with a mild degree of pyrexia but with no gross fever or constitutional signs. The intensity of pain and disability is not comparable to similar lesions in other parts of the bony skeleton. The degree of pain is characteristic of cartilaginous involvement in joints. In an acute gonorrheal joint the pain is pathognomically intense and here the brunt of the pathological changes falls on the cartilage.

4) The fourth unusual feature is the evidence of bony changes with a primary affection of the symphysis, a tendency to bilateral involvement of the other bones of the pelvis associated with gross rarefaction and complete reconstitution of the bony structure following on cure of this self-limited disease.

5) The almost complete lack of response to all therapeutic procedures in a disease that proceeds to resolution is anomalous and rarely seen in other conditions.

Approaching the problem from the appearances presented radiologically the characteristic early finding is that of rarefaction. The rapid onset of decalcification in a bone demands the presence of marked hyperemia. This may rise from three main causes: a) infection within the bone, b) infection adjacent to the bone, and c) interference with the nervous supply of the blood vessels to the bone. Rarely is it possible for vitamin or hormonal upsets to produce a similar condition. The suggestion of Beach that all of these cases occur as a result of a "septic spill of urine" is an obvious one considering the operative factors preceding the complication. He envisages a gross infection of the prevesical space, stating "this clinical entity is dependent on an accumulation of urine or septic material behind the pubes overspreading the nutrient foramen." It is hard to believe that infection could be present in soft tissues and yet no clinical evidence of such be consistently present. In a very few cases in my series was there any record of soft tissue involvement. He further suggests closure of the bladder and lack of adequate drainage as predominant factors, but surely again infection in the prevesical space with its abdominal cellulitis and constitutional disturbance would be recorded prior to the 15–28 days that osteitis generally takes to evidence itself. In most of the cases osteitis pubis appeared in the presence of a soundly healed abdominal wall. That an inflammatory origin for the lesion is suggested by the intensity of the pain and the amount of destruction of tissue is not denied. One would however, expect as in other bony infections associated with marked pain a gross amount of constitutional disturbance with greater temperature rise. Further, one queries why an inflammatory lesion should be predominantly bilateral and slowly and symmetrically progressive. Many writers have suggested trauma as the main etiological factor. Beer suggested that direct trauma by the pressure of retractors or drainage tubes or periosteal injury from avulsion of the fibres of attachment of the rectus muscle may provide the cause. Kirz (1947) described three factors which may be responsible: 1) The deliberate opening of the prevesical space; 2) avulsion of the fibres of the rectus muscle or of the two layers of the transversalis fascia attached to the pubic bone; 3) rupture of the puboprostatic ligaments in the process of enucleation of the prostate.

Added to these with the increase in popularity of the retropubic operation, the possibility of a needle prick of the periosteum has been suggested. This complication, however, has occurred in the practice of surgeons who never use anterior retractors in the wound, who always insert their drainage tubes in the upper angle of the wound, who feel certain that gentleness in handling of the rectus muscle or transversalis fascia precludes any damage to these structures and who do not tear the prostate out of its capsule. It has been suggested that perhaps this condition arises from damage to the nutrient vessel of the pubis. Pathologically this tenet is insecure since necrosis and sclerosis of bone would result with few or none of the clinical signs and symptoms of osteitis pubis.

Wheeler (1941) rejected the inflammatory theory as a result of his failure in a series of experiments on animals to infect the pubis or periosteum with over-infected urine. He preferred to ally the condition with that interesting complication of trauma to the extremities known as Sudeck's post-traumatic atrophy. Bruskewitz and Ewell (1949) also favor this explanation. At a varying period of time after even a slight injury the patient presents a typical syndrome. Complaint is made of marked pain out of all proportion to that suffered with the original injury and unrelieved by immobilization. With this are associated trophic changes in the limb distal to the injury: edema and blueness of the hand and foot. The bones in the vicinity showed marked spotty osteoporosis. Following on this there is gradual destruction of cartilage which may eventually lead to a fusion of joints and a useless extremity when recalcification eventually occurs. The cause of this condition is accepted as being due to interference with the nerve supply to the blood vessels of the part producing gross hyperemia and a consequent washing out of the calcium of the bones. Improvement has been achieved from the operation of periarterial sympathectomy.

The inexplicable onset, the prominence of pain as a clinical feature and the gross osteoporosis suggest a similarity between it and osteitis pubis. However, the two conditions do not correspond accurately. The pain of Sudeck's atrophy is not relieved by rest, rather any form of fixation increases it. On the other hand, in osteitis pubis the emphasis is on acute distress on attempt at movement, and avoidance of this appears to produce amelioration of the pain. Secondly no trophic changes are seen over the pubes in the soft tissues. This may of course be relative to the thickness of the tissues and the distribution of the arterial supply. Further the pain of Sudeck's atrophy is relieved by radiotherapy even though this treatment bears no relation to the course of the disease.

Two cases of Millin's series have exhibited similar radiological changes in the vertebral column to those in the pubes. This has led him to suggest that the condition develops in some way through the pelvic veins associated as they are with the vertebral series. Batson (1940) demonstrated in his work on the venous system of the pelvis and its relationship to metastases in prostatic carcinoma that if a thin medium were injected into the dorsal vein of the penis a spread was seen to the ilium, to the veins of the pelvic girdle, to the veins of the vertebral system even to the sinuses of the skull. Millin has suggested a venous spread of infection by this route as an explanation of this occurrence.

In conclusion, it is stressed that osteitis pubis is an increasingly common complication of operations on the lower urinary tract. It is believed that the actual pathology remains unsolved, all the various theories evolved being inadequate in their explanation. As the condition, in the vast majority of cases, appears in association with the opening of the bladder early care should be taken to avoid any of the possible factors that have been mentioned as causative elements until the exact etiology is understood.

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REFERENCES

Batson, O. V.: Ann. Surg., 112: 138, 1940.
Beer, E.: J. Urol., 20: 233, 1928.
Beach, E. W.: Urol. & Cutan. Rev., 53: 577, 1949.
Bruskewitz, H. W. and Ewell, G. H.: Arch. Surg., 77: 705, 1949.
Kirz, E.: Brit. J. Surg., 34: 272, 1947.
Millin, T.: Personal communication.
Wilensky, A. O.: Arch. Surg., 37: 371, 1938.

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OSTEITIS PUBIS: ITS ETIOLOGY AND PATHOLOGY

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Osteitis pubis is no longer a rare complication of suprapubic prostatic surgery. In 1945, Maurice Muschat, in a comprehensive study of the literature, was able to discover but 25 cases including the original cases of Edwin Beer. Since that time, Kirz reported 10 cases, we reported 7, Vest reported 7, and Moore 8, Beach reported 7, and Mortensen 38, among others. Why the increased incidence of this disease? Was it previously unrecognized? One could hardly fail to overlook this complication as the patient is totally incapacitated for a long time and the psychic trauma is apparent. Has the retropubic method of enucleation of the prostate gland as popularized by Millin been a factor? We believe not. We believe that our pathological and bacteriological investigations shed some light on the etiology of this disease. This paper will disclose the biopsy findings of 3 patients who were in the acute stage of osteitis pubis.

Osteitis pubis is known under a large variety of names, yet it is a very distinct clinical entity which follows a definite course and presents clear cut clinical and roentgenological features. It has been called periostitis pubis, osteochondritis pubis, panosteitis pubis and osteoporosis of the pelvic bones or the acute bone atrophy of Sudeck. Sudeck's atrophy is not an infectious process. Our studies show that osteitis pubis is a chronic inflammatory disease. Wheeler in 1941 could not reproduce the disease in rabbits by injecting sterile urine under the periosteum, by injecting urine infected with Staphylococcus hemolyticus aureus, by trauma to the periosteum or by the combination of trauma to the space of Retzius and the injection of infected urine. He concluded then that the disease commonly known as osteitis pubis was noninflammatory, nontraumatic, and that it should be called a Sudeck's atrophy of the anterior pelvic girdle. Cohen in 1946 agreed with the concept of an aseptic process of the Sudeck's atrophy variety because it failed to respond to chemotherapy. In 1947, Bruskewitz and Ewell agreed with Wheeler and Cohen that the condition is an acute bone atrophy. Our studies show that the complication is a chronic inflammatory disease of the bone, cartilage and periosteum of the pelvic girdle and is of bacterial origin. We believe that the name osteitis pubis should be retained as it fairly describes the inflammatory nature and location of this disease.

This paper concerns itself with the pathological and bacteriological findings in 3 cases, all of which followed retropubic prostatectomy, and with the autopsy study of a healed case, that of a man who died 18 months later of another disease. In the 3 cases in which tissue was obtained, a clinical diagnosis of osteitis pubis was made and confirmed by the roentgenological findings. The biopsy material was obtained in the following way. An incision was made over the symphysis pubis and carried down through the skin, subcutaneous fat and fascia down to the periosteum of the symphysis. A deep wedge of the periosteum, cartilage and

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bone of the anterior portion of the pelvic girdle was taken either by a scalpel or by a chisel and hammer. Half of the tissue was put aside for studies in the Department of Pathology, and the remainder was given to the Bacteriology Department for aerobic and anaerobic cultures. Certain findings were noted in each case. Between the skin and periosteum no disease was found. There was no fluctuation, edema, induration or necrosis. The periosteum in each case was white and glistening and appeared normal. However, immediately upon cutting into the periosteum it was evident that we were treating with soft, spongy material on which some masses of granulation tissue were interspersed. A small amount of thick, grayish material was also recognized in the bony substance.

In each of the cases an abundant growth of Pseudomonas aeruginosa was found. In one case, in addition to Pseudomonas, the Proteus vulgaris was cultured out as a mixed infection. No growth could be obtained from any of the anaerobic cultures in 3 days. However, after transplanting some of this material on aerobic cultures a growth of gram-negative rods was re-obtained. Hence, in 2 cases a pure culture of Pseudomonas aeruginosa was obtained and in the third patient a mixed infection of Pseudomonas aeruginosa and Proteus vulgaris existed.

The material submitted for culture was in the form of soft spongy tissue, and was planted routinely on blood plates, agar slants, beef heart broth, brain beef heart broth and blood serum media. Cultures grown under aerobic conditions showed gram negative rods, 0.6 by 1.5 microns long occurring singly, in pairs, and in short chains. Slight motility was observed. Colonies on agar were large spreading, grayish with dark centers and translucent with an irregular edge. The growth was abundant and the medium turned green. On blood plates the growth was abundant and produced hemolysis. The broth showed marked turbidity with a thick pellicle and heavy sediment. On blood serum media good growth was obtained with greenish color and partial digestion of the media. All the cultures had a marked odor of trimethylamine. The green pigment "pyocyanin" could be extracted with chloroform and with water. These characteristics are those of Pseudomonas aeruginosa.

Cultures in one case (R. V.) showed besides the Pseudomonas aeruginosa another type of gram-negative organism, 1.0 by 2.5 microns long occurring in pairs and long chains. On agar the colonies were opaque, gray and spreading. Broth showed marked turbidity with a thin pellicle having a putrefactive odor. On Kligler's iron agar it produced hydrogen sulfide. The gram negative staining rods were pleomorphic and the organisms in drop preparation showed good motility. This organism was, therefore, identified as Proteus vulgaris. Both organisms are common habitants of the normal skin particularly in the hairy areas. Dr. Louis Nerb, head of the Bacteriology Department of the Brooklyn Hospital, made the studies on the biopsy material.

Meleney states in his recent *Treatise of Surgical Infection* (p. 223) that "the Pseudomona is of interest to the surgeon chiefly because of its frequency as a contaminant of surgical wounds. Only rarely is it found to produce evidence of pathogenicity. Such infections generally occur in debilitated individuals." Medical bacteriologists have been accustomed to refer to this organism as a member of the Pyocyaneus group, taking the name from the long-known type species, Bacillus pyocyaneus, or bacillus of blue pus. They are widely distributed in nature, being found in water, soil, and intestinal contents of man and animal. Although the Pyocyaneus is one of the less virulent pathogenic bacteria in man, it has been found in suppurative lesions of the body. Often, it is a mere secondary invader in the wake of another inciter, but occasionally it is found as the primary cause of inflammation. Thus, Pyocyaneus has been found as the cause of otitis media and diarrhea in children. It has been cultivated from the spleen at autopsy from a case of general sepsis following mastoid operation. It has been found in pericardial exudate and in pus from liver abscess. The Pyocyaneus has been found in prostatic abscesses and in pyelonephritis. This organism produces both an endotoxin and an exotoxin. While the true exotoxin of Pyocyaneus is like that of diphtheria and tetanus, it never approaches the strength of the diphtheria and tetanus exotoxin.

The primary pathogenicity of Proteus vulgaris is slight, but as a secondary invader of infected wounds, mucous membranes and cavities of the body it plays a role of considerable importance. In cystitis and pyelitis associated with urinary calculi or following obstruction of the urinary tract, Proteus vulgaris is often present and appears to be in part responsible for the pathological effects.

PATHOLOGY

Dr. J. Arnold deVeer reported that the tissue was distorted by fibrosis and presented subacute chronic inflammation involving the periosteum, bone and cartilage. Several nerves with advanced degenerative changes and proliferation of sheath cells were seen. The inflammatory infiltration included plasma cells and eosinophils in large numbers. No suppuration was seen, but the entire process suggested infection of low virulence and of long standing.

CLINICAL DIAGNOSIS

Three to seven weeks after a prostatectomy when the patient is at home and walking about, he is suddenly seized with pain over the symphysis pubis. In a few days the pain becomes excruciating and involves one or both pubic rami. The patient experiences great difficulty in locomotion because of pain along the inner aspect of the thighs caused by spasmodic contractions of the adductor magnus. There is no swelling or redness in the pubic region, but tenderness over this area is exquisite. X-ray corroboration is not obtained until four to thirteen weeks after the prostatectomy. A low-grade febrile reaction, a moderate leukocytosis, polycytosis and secondary anemia are generally present. The clinical aspects of these cases are presented with a minimum of details. The major concerns of this paper are with the bacteriologic and pathologic features of osteitis pubis. The disease does not respond to the present day chemotherapeutic or antibiotic agents. It is a self-limiting disease with complete recovery in three to nine months.

CASE REPORTS

Case 1. R. V., aged 72, underwent retropubic prostatectomy on November 26, 1948. The pathological diagnosis was carcinoma of the prostate. Symptoms of osteitis pubis began 5 weeks after operation. X-ray evidence was positive on February 16, 1949. Biopsy was done 12 weeks after the original operation. Culture of biopsy material revealed Pseudomonas aeruginosa and Bacillus proteus. Pathologic report of microscopic study of the biopsy material revealed that chronic inflammation was present in several foci of the periosteum. Fibrosis also involved the marrow spaces. At a site of tendinous insertion, on its outer surface, that is, away from the bony insertion, some granulation tissue was found. There was no evidence of gross suppuration (fig. 1, *A*).

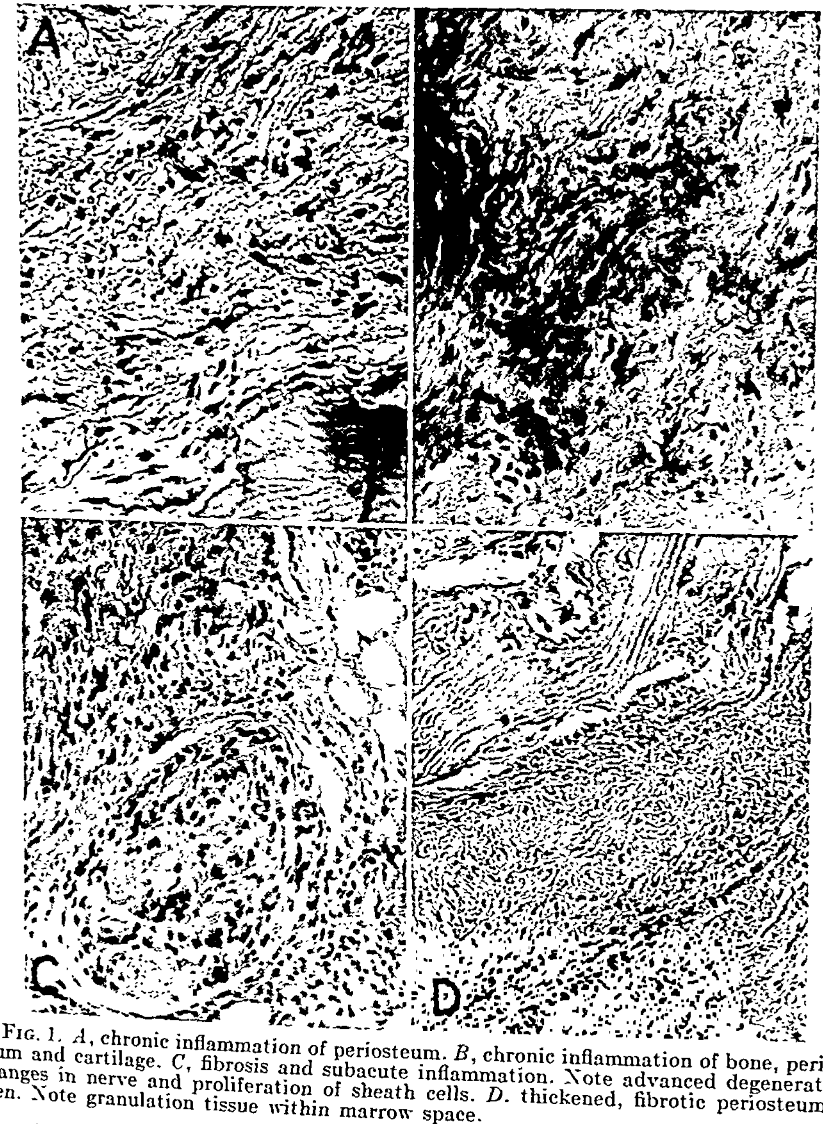

FIG. 1. *A*, chronic inflammation of periosteum. *B*, chronic inflammation of bone, periosteum and cartilage. *C*, fibrosis and subacute inflammation. Note advanced degenerative changes in nerve and proliferation of sheath cells. *D*, thickened, fibrotic periosteum is seen. Note granulation tissue within marrow space.

Case 2. W. C., aged 68, underwent retropubic prostatectomy on May 28, 1948. The pathologic diagnosis was benign prostatic hypertrophy. Symptoms of osteitis pubis began on June 23, 1948, and x-ray corroboration was obtained on July 16, 1948. Biopsy of the symphysis pubis was done on July 22, 1948, or 8 weeks after the prostatectomy. Microscopic sections revealed chronic inflammation of bone, cartilage, and periosteum. Bacteriological studies of the submitted material revealed a growth of Pseudomonas aeruginosa in pure culture. See figure 1, *B*.

Case 3. G. McD., aged 60, underwent retropubic prostatectomy performed on November 10, 1948. The pathological diagnosis was benign prostatic hypertrophy. On February 2, 1949, the patient began to have pain over the left pubic rami and adductor spasm which interfered with his ability to walk or move in bed. X-ray evidence of osteitis pubis was noted 1 week later and a biopsy of the left pubic bone was done on February 11, 1949. Pathological examination revealed that the bone was spongy and very friable. The tissue was distorted by fibrosis and subacute inflammatory infiltration. Several nerves revealed advanced degenerative change with proliferation of sheath cells. The bacteriological studies revealed Pseudomonas aeruginosa in pure culture. See figure 1, *C*.

Case 4. P. F. was aged 72. His early course was discussed in a previous paper. On December 21, 1947, a one stage suprapubic prostatectomy was performed. The diagnosis was benign prostatic hypertrophy. Symptoms of osteitis pubis began 5 weeks later with complete recovery in 3 months. The patient returned to the hospital on January 3, 1949, with a fulminating tetanus infection of a leg varicose ulcer. Death occurred on January 5, 1949. At autopsy, the major portion of the prostate gland was absent as a result of surgery. There were dense adhesions at the prevesical bed which anchored the bladder to the symphysis. The decalcified pubic bones on microscopic section revealed thickened fibrotic periosteum and granulation tissue within the marrow spaces. See figure 1, *D*.

PREVENTION

Meticulous care in the preparation of the skin for operation is necessary to rid the genital area of these organisms of so-called low pathogenicity. It is realized that complete sterilization of the skin in actual practice is virtually impossible and that asepsis is a relative term. The preparation of the patient for prostatic surgery since the discovery of these pathological and bacteriological findings has consisted of a hot, soapy shower or bath the night before operation. On the operating table, a 5 minute scrub using green soap to the lower abdomen, scrotum, penis and thighs is done. The suds are removed with sterile water, the skin then dried, and followed with ethyl ether. Only after the latter step is taken is the regular tincture of merthiolate preparation of the skin for the incision made.

DISCUSSION

Since 1945, we have studied 11 cases of osteitis pubis and for the last 8 months or since the institution of the above skin preparation, we have enjoyed the longest respite from osteitis pubis and we hope that this meticulous skin preparation will solve our problem and spare our patients of this most distressing complication.

We believe that this study represents the first bacteriological investigation of the diseased portion of the symphysis and pubic rami. We, ourselves, intend to perform no more biopsies as the healing time required for the closure of these sinuses has run between 4 and 6 weeks which has caused additional discomfort to the patient and a prolonged hospital stay.

SUMMARY AND CONCLUSIONS

Osteitis pubis is true inflammatory disease of the anterior pelvic girdle and not a sterile necrosis of bone as in Sudeck's atrophy. In a study of three biopsied cases the causative organism was found to be the Pseudomonas aeruginosa in each case and in association with the Bacillus proteus in one case. These gram-negative organisms are bacteria of low virulence and low pathogenicity. This, in our opinion, explains the long incubation period between the prostatectomy and the onset of symptoms of osteitis pubis. More biopsies in other cases will be, needed to show whether other organisms can produce this disease.

The pathology consists of subacute inflammatory infiltration and chronic inflammation involving the periosteum, bone and cartilage. Plasma cells, eosinophils and granulation tissue are seen in the inflammatory tissue.

All of the known sulfonamides and antibiotic agents were tried and none found to be specific. The treatment, we are convinced, should be prevention. Whether the skin is prepared with green soap or the newer antiseptic deturgents, should be up to the operating urologist, but we are convinced that the ordinary preoperative painting of the suprapubic region is not sufficient to prevent osteitis pubis.

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REFERENCES

ASCHNER, P.: J. Urol., **12**: 259, 1924.
BARNES, F. L.: Texas State J. Med., **28**: 601, 1933.
BEACH, E. W.: Urol. and Cutan. Rev., **53**: 10, 577, 1949.
BEER, E.: Int. J. Med. & Surg., **37**: 224, 1924.
——: J. Urol., **20**: 233, 1928.
BRUSKEWITZ, H. W. AND ELWELL, G. W.: Am. J. Surg., **77**: 705, 1947.
COHEN, H. H.: J. Urol., **55**: 84, 1946.
GOLDSTEIN, A. E. AND ABESHOUSE, B. S.: Surg., Gynec. & Obst., **49**: 477, 1929.
—— AND FERBER, W. L. F.: J. Mt. Sinai Hosp., **4**: 1052, 1938.
—— AND RUBIN, S. W.: Am. J. Surg., **74**: 480, 1947.
KIRZ, E.: Brit. J. Surg., **34**: 272, 1947.
KLEINBERG, S.: J. Urol., **48**: 635, 1942.
KRETSCHMER, H. L. AND SIGHTS, W. P.: J. Urol., **23**: 573, 1930.
LAVALLE, L. L. AND HAMM, F. C.: J. Urol., **61**: 83, 1949.
LAZARUS, J. A.: Ann. Surg., **103**: 310, 1936.
MUSCHAT, M.: J. Urol., **54**: 447, 1945.
PEIRSON, E. L.: Surg., Gynec. & Obst., **49**: 834, 1929.
POWELL, N. B.: J. Bone and Joint Surg., **29**: 785, 1947.
SILVER, C. M.: Bull. of Hosp. for Joint Dis., **2**: 10, 1941.
WHEELER, W. K.: J. Urol., **45**: 467, 1941.
WILENSKY, A. C.: Arch. Surg., **37**: 371, 1938.

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DISCUSSION

DR. SAMUEL A. VEST (Charlottesville, Va.): It is a pleasure to hear our good friend, Mr. Mortensen, who is back with us again. I recall his presence here at a previous meeting, especially at a time when osteitis pubis had begun to appear with an amazing instance in this country. Let us hope that he did not transport the noxious agent back to Australia because he certainly has returned with quite an array of cases. With the many instances which he reports from that continent we are now not alone in experiencing this condition.

Mr. Mortensen's presentation has well described the clinical course of disease and quite adequately surveyed the etiological possibilities. This unusual condition is so extraordinary that it would not be amiss to summarize the following significant features here. The amazingly frequent occurrence of a hitherto rare disease in the last 3 years of the twenty-six since its first recognition. My associate, Dr. Rosenberg and I reported 4 cases occurring in a space of several months at our clinic, two following retropubic prostatectomy and two following transurethral resection. Since 1948, we have encountered two additional instances following retropubic prostatectomy making a total of six. It was extremely rare before that time and in observing and participating in several thousand operations on the prostate I was not even aware of the complication. It is now not an uncommon disease whereas it was a most unusual occurrence following the tens of thousands of prostate operations that had been done in the 60 years before 1947. It is a significant fact that the condition is almost synonomous with disturbances in the sub-pubic space. Why does it not occur following perineal prostatectomy and especially radical perineal prostatectomy in which the sub-pubic space is widely exposed, the puboprostatic ligaments are divided along with removal of fat, nerves and lymphatics in this area? Certainly the symphysis is traumatized with tractors during this particular procedure. One might gather from such an analogy that dependent drainage in perineal surgery is a factor when compared to the other three approaches to the prostate. The condition is a bilateral involvement of the symphysis. The exact nature of this distressing disturbance is extremely obscure. The latent period from the time of the operation to the sudden onset may be a delay of weeks to upwards of four months, a most extraordinary and mysterious circumstance. Why should it appear in the last 4 years when one considers all the previous trauma and infection of the subpubic space in the previous 60 years? A significant feature is the change in the cartilage and it should perhaps be more properly termed a periosteochondritis. It is a condition which has been singularly resistant to all types of therapy, especially the antibiotics. These, in brief, are the seven outstanding features of this disease state.

In our series we felt confident in the first cases that there was an infection adjacent to the undersurface of the symphysis. We opened these cases but found no evidence of infection and encountered a perfectly smooth and normal periosteum covering the symphysis just as one encounters in total cystectomy or radical perineal prostatectomy. If this is an infectious disease there is hardly but one logical assumption. One must speculate that a hitherto unknown microbe has appeared or that an organism has developed which is resistant to no one of the antibiotics and which actually resulted from attenuation or mutations following contact with modern antibiotics as used in therapy. The behavior of organisms in such a manner in which they become attenuated is well known in vitro but no clinical data of which I am aware have been presented. In the laboratory, organisms become attentuated but not for long after withdrawal from contact with the antibiotic. There is certainly no other clinical evidence of such phenomenon or any new reported disease.

In respect to trauma, Mr. Mortensen speaks of interruption of nutrient arteries. According to orthopedic information, the interruption of blood supply to bone by division of nutrient arteries results in a condensation process at first and this does not occur in osteitis. This fact and the common trauma to the symphysis over the last six decades would not argue toward this end. It is of interest at our institution that two and three years ago the orthopedic department had two mild cases of osteitis pubis. These occurred in football players during the regular season and were accompanied by x-ray changes.

If this condition is one of autonomic neurovascular disturbance, such as Sudeck described for other bones, I wonder if Mr. Mortensen knows of any interruption of the abdominal sympathetic chain either by surgery or alcohol necrosis? Would such treatment reverse vascular disturbances or blood flow in the symphysis and favorably affect the course or symptomatology? I have heard of one case in which ACTH dramatically cured this condition and in fact this has been the only instance in which there was any effective therapeutic agent as far as I am aware. If this effect is further substantiated it would support the thesis that so-called osteitis pubis is not an infectious process but is some metabolic or nutritional disorder. I would also like to ask Mr. Mortensen if the whole gamut of autonomic drugs has been fully explored with the object of regulating an alleged disturbed blood supply.

Dr. Edward W. Beach (Sacramento, Calif.): The authors have offered a worthy contribution to the subject of osteitis pubis which currently basks in the urological limelight. Theirs is the fifth paper within the year to treat of this enigmatic entity and the total number of cases I now know of is one hundred twenty-eight. Without a question, many more cases have never been recorded.

The time has come to attempt more precise definition with regard to osteitis pubis which presently reposes in "confusion worse confounded"—in many of its phases—not only as to etiology but anent exact connotation of the term itself. The latter is loosely used and means a different thing to different clinicians. For instance, at the February meeting of the American Academy of Orthopedic Surgeons, iliac osteitis cystica (decalcification of the iliac bone adjacent to the sacro-iliac synchrondrosis often noted in the aged) was discussed in relationship to osteitis pubis and it was held by some that these two morbid processes were identical save for different areal expression. Klinefelter described a post-traumatic condition in a 16 year old boy in whom the x-rays showed dimineralization and spotty destruction of the right pubis—superior and inferior rami—with extension into the ischium.[1] This he calls osteitis pubis. Recently, an obstetrician referred to me a woman who had sloughing osteomyelitis and sinus of the pubic bone following episotomy which he insisted was osteitis pubis.

The etiology has always been the sixty-four dollar question and it still is, in my opinion. Some submit it as evidence of Sudeck's atrophy and speak of aseptic necrosis. Others accept the inflammatory concept but quibble with regard to bacteriologic aspects—since this process, unlike osteomyelitis always terminates in resolution with normal bone contour and histologic architecture (Wheeler)[2] in due course despite any or all therapy. Still others stress the role of trauma. Millin blames the boomerang needle but in remote California sheep country, our surgeons have not yet heard of his weapon. Henderson[3] defends the infection idea and thinks osteitis pubis may represent a metastatic process from the prostate.

To add to this chaos, to some, osteitis pubis is always bilateral; to others it may be unilateral. To most of us it represents a sinister postoperative complication. *In this paper the authors stress the point that osteitis pubis is a chronic* infection. Others believe it is a smoldering, slowly progressive acute or subacute affair. The time of onset in postoperative cases is set forth by some as 10 to 12 days but others feel the prodromal period is 4 to 5 months. Again, that confusion deal.

To me, *osteitis pubis represents an orthopedic disease sponsored by urologic surgery.* I have studied clinically now 14 cases, seven of which I reported last year.[4] Widespread interest in this subject is attested by some 56 letters of inquiry which came to hand soon after this publication appeared.

Because of this baffling etiological question I had some anatomic dissection made to discover whether the source of infection could be a puddle of urine collected retropubically overlying the foramena of the nutrient pubic blood vessels. This work directly revealed that the blood vessel distribution in this region was most variable and inconstant and sometimes almost entirely unilateral. Perhaps herein lies the factor which determines whether development is mostly unilateral or bilateral in a given instance.

I took biopsies in four of these 14 cases. In all a panosteitis i.e. involvement of all layers of the bone, existed. All biopsy wounds healed rapidly and within 10 days.

Four of these cases of osteitis pubis followed transurethral resection—no open surgery done.

Anent the bacteriologic aspects, one wonders whether Pseudomonas auerginosa (B. pyocyaneus) and *Proteus vulgaris* should be stressed. These organisms are extremely widespread and not highly pathogenic. While I was on the Solomons Islands, we had an epidemic of "jungle rot" involving the external auditory canal and we cultured B. pyocyaneus from every case, some 87. Moreover, this same organism flourished in the stagnant river waters, even in the sea water at the mouth of these rivers, not to mention the "hog wallow" soil, as cultures proved.[5] It bears mention too that if these organisms are the real culprits in osteitis pubis, then Parke Davis and Company slipped a cog in their experimental work on chloromycetin which is supposed to give excellent results against Pyocyaneus and Proteus.

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[1] Klinefelter, E. W.: Am. J. Roentgenol., **63:** 368–371, 1950.

[2] Wheeler, W. K.: J. Urol., **45:** 467–475, 1941.

[3] Henderson, D. St. C. L.: Brit. J. Urol., **22:** 40–51, 1950.

[4] Beach, E. W.: Urol. & Cutan. Rev., **53:** 577–584, 1949.

These authors have done well to emphasize preoperative preparation and cleanliness. Not so long ago, a green soap poultice for 12 hours to the preoperative belly was insisted upon; if no poultice, then no operation. Maybe it was expedient for osteitis pubis was not recounted nor recognized in those days.

Perhaps these authors have supplied us the missing piece in this etiologic jig-saw puzzle; let us hope so. Difference of opinion, however, makes a horse race and in the light of our present knowledge concerning osteitis pubis, I still think it must be pegged among those things which "we know not, and which remain too wonderful" for us; yea, one which defies current explanation.

Dr. Archie L. Dean (New York, N. Y.): Last February when I was fortunately away from home, a patient of mine in Memorial Hospital, on whom I had performed a rather extensive resection of the anterior wall of the bladder for cancer, developed osteitis pubis. My associates gave the patient adrenocorticotropic hormone, 100 mg. a day for 4 days. Previously, at the end of 3 hours, he would cry out in his pain for another quarter of a grain of morphine. After the second injection of the ACTH, his pain was gone.

There was an interval of 4 days after the end of this treatment. Then he was given a similar course, lasting 4 days. This benefit was much more than the usual euphoria which follows the administration of this medicine, because the patient promptly began to walk about and his improvement clinically and roentgenologically has been steady ever since. He has required no more morphine and he has required no more ACTH.

While one swallow doesn't make a summer, the number of agents which have been successful in the treatment of this painful and disabling condition have been so few that I recommend a trial of this medicine, when it can be obtained.

Dr. Thomas D. Moore (Memphis, Tenn.): These two papers have been very illuminating. The clinical picture of osteitis pubis, as revealed in Mr. Mortensen's excellent paper and the findings of the bacteriologic and pathologic investigations carried out by Dr. Lavalle, will be received with universal interest among urologists.

It has been my misfortune to have had this complication to occur in 13 instances, all of which followed retropubic prostatectomy. It is rather remarkable that in 159 consecutive retropubic prostatectomies, this complication occurred 13 times among the first 80 and has not occurred among the last 79. This experience caused us to pause and take stock in order to determine, if possible, just what factors might be responsible for the sudden disappearance of this complication since August 1948.

We found that there were some comparatively insignificant changes in technique at that time. Prior to that, for instance, the prostatic capsule had been routinely incised with an electric scalpel. Since then, however, the capsule has been divided with an ordinary scalpel between hemostatic sutures along with the avoidance of electrocoagulation of the veins comprising the plexus of Santorini. Also a soluble sulfonamide containing 5,000 units of streptomycin per 100 cc was used locally as a prophylactic. In view of Dr. Lavalle's observation that a bacillary infection of low degree is present, the use of the antiseptic might have been a possible factor. The late onset of the complication in our experience has been interesting. It varied from 2 weeks to 5 months, averaging 2 months postoperatively in the 13 cases. In nearly all of these the incision had healed per primam. From the standpoint of therapy we were stimulated to employ deep roentgen therapy at the suggestion of Dr. Vest. One of these patients who had osteitis pubis of moderate degree with symptoms present for approximately three weeks was re-admitted to the hospital and after only two treatments consisting of a total of 300 r units, he was able to walk out of the hospital about a week later. Roentgen therapy in subsequent cases was tried with definite benefit and it is my impression that of all the therapeutic measures suggested so far, it has proved to be the most valuable single measure in our experience.

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[5] Beach, E. W. and L. L. Hamilton: U. S. Nav. M. Bull. 44: 599-602, 1945.

DR. JOSEPH F. McCARTHY (New York, N. Y.): I don't like the job I have of being critical of Terence Millin's operation, of whom I am very fond, not of the operation but of Mr. Millin. But one criticizes a brother. Therefore I take this latitude.

Obviously, there was here introduced, not one operation but two. The first and last paper on osteitis pubis that I recall hearing read before this society, was in Edwin Beer's time. Now, we find a marked increase of osteitis pubis. Obviously, this delightful object of our retrospective ruminations, the prostate gland, has been, is, and will continue to be a bone of contention.

It is a matter of common observation that the average individual likes to do that which he thinks he does best. This may be sitting on a pole or going down the rapids in a barrel. For similar reasons, the same tendency applies to the enthusiasm that has prevailed in the past two years concerning this method. It has never appealed to me, first because it violates every principle of prostatic surgery. There is no excuse for osteitis pubis in this field.

Our approach to the prostate is made on a fairly full bladder, with an indwelling catheter and a loaded syringe. A transverse incision 5 cm. above the symphysis, 5 cm. in extent, with a sharp approach down to the bladder through the fascia transversalis, exposing the bladder, then further filling it under view as well as by palpation. This obviates opening of cellular spaces and prevents infection. The wide exposure, vascular ligation and incidental damage to the vesical neck and urethra in the retropubic operation, are opposed to all our teaching concepts. This does not necessarily mean that our teaching of the moment should continue to prevail, but this method is against common sense—common surgical sense.

The position of the patient should be, in my opinion, the lithotomy position.

The dorsal position is illogical for a suprapubic prostatectomy. Prepare the patient both perineally and abdominally: enucleate the prostate, pack the cavity with hot gauze for 5 to 10 minutes to arrest venous bleeding: then pass the visualized electrotome per urethram and the arteriolar bleeders are clearly visualized and electrocoagulated. By this technique, compression bags or packing should not be necessary.

I wrote a paper on this procedure some two or three years ago, tried it a few times, could not sell it to my associate, Dr. Ritter, who tried the retropubic operation and got in plenty of hot water.

Dr. Abe Hyman, who is in this audience, can elaborate on the clinical results, and it is my hope that the combination of McCarthy and Hyman may add further enlightenment to this subject.

Finally, I do not go along with the present trend of complete closure. Our practice is to close the original incision, but before doing so, one should buttonhole the bladder at a nearby site, with a Kelly clamp and draw through a right angle whistle-tip catheter for drainage, and as a safety valve for two or three days until the danger of early bleeding is over.

DR. PAUL W. ASCHNER (Brooklyn, N. Y.): I had the great privilege in the 1920's to be closely associated with the late Dr. Edwin Beer. When I was on service with him at the Mount Sinai Hospital, New York, we first observed the cases which he designated periostitis pubis.

At a meeting of the Section on Genito Urinary Surgery, New York Academy of Medicine, January 16, 1924, Dr. Beer briefly reported the clinical picture and early x-ray findings. He noted that it followed suprapubic prostatectomy (3 cases) and partial cystectomy for carcinoma (1 case).

At a meeting of The American Urological Association, June 1924, I presented "Observations upon Suprapubic Prostatectomy" in which 365 cases of prostatic hypertrophy were reviewed. Four cases of periostitis and ostitis pubis were reported by me in this study with a description of its clinical features and roentgen findings. One case occurred among 44 one-stage procedures; 3 cases occurred among 233 two-stage procedures.

Strangely, it often occurs in patients who have a benign postoperative course, with no gross infection of the wound and no unusual infection of the urine drainage from the wound. Frequently the patient has healed faster than usually. Three or four weeks, or perhaps as many months after operation, the clinical picture so admirably described by Mr. Mortensen supervenes. In our first cases our impulse was to suspect that the pathologist had erred and missed a carcinoma of the prostate and we called upon him to review his material.

Subsequently the same complication was observed after partial cystectomy for neoplasm. In May 1940, I saw in consultation with Dr. Theodore L. Cohn a woman of 53 suffering from severe acute B. coli pyelonephritis of the right kidney. This responded to sulfanilamide therapy but a month later I was called again and found that she had periostitis and ostitis pubis of hematogenous origin. Not relieved by resumption of sulfanilamide therapy she was seen about two weeks later by the orthopedist, Dr. Samuel Kleinberg. He concurred in my diagnosis, and immobilized the pelvis and lower extremities with a plaster spica. She obtained relief and eventually recovered completely. Dr. Kleinberg reported this case in the *Journal of Urology* (vol. 48, p. 635, 1942).

As to etiology it is my belief that trauma opens the pathway for organisms of low virulence in the urine to invade the periosteum and the fibrocartilage of the symphysis pubis, and thence to spread to the adjacent bones. As to prevention it is my belief that a liberal incision is the first requirement; secondly, that if a midline suprapubic approach is made, one should take care to leave the apex of the pyramidalis attached to the linea alba, and its base to the pubic bone. By entering the prevesical area lateral to either pyramidalis, one avoids exposing the structures vulnerable to trauma and contamination. But the pyramidalis may be absent and therefore this potential ally is not always available. Thirdly, the forceful spreading apart of the recti by self-retaining retractors is to be avoided. It seems probable that the high incidence of this complication reported by some operators after retropubic prostatic enucleation is ascribable to the use of such retractors and the tendency to spread them widely and forcibly in order to get enough room to work down behind the symphysis.

Fortunately neither I nor my associates have had a case of periostitis pubis following the retropubic procedure but I suppose it will come and it would seem more likely to occur when closure of the capsule has not been water tight, thus permitting urinary leakage and resultant infection of the pelvic cellular tissues and endopelvic fascial planes. (My first case greeted me on my return from Washington. He had no leakage, healed per primam, and was discharged from the hospital in 8 days.)

The most recent case I saw was at the Beth El Hospital. The patient underwent a transurethral resection at a municipal hospital 2 months previously. Immediately following the procedure he had experienced intense lower abdominal pain, chill and high temperature. In addition to the periostitis pubis his urine was infected and he was incontinent. I believe that his prostatic capsule had been violated and thus there occurred spread of infectious material to the pelvic cellular tissues and fascial planes.

Although this entity was described more than 25 years ago, many urologists and orthopedists have only recently become aware of it, and thus it appears to be occurring more frequently.

The efforts of Drs. Lavalle and Hamm to throw more light upon its etiology and pathology are indeed timely and welcome. At my suggestion Dr. Carroll M. Silver, resident at the Hospital for Joint Diseases reported four cases in the Bulletin of that Hospital (vol. 2, p. 10, 1941). In case 2 biopsy of the left ischial tuberosity yielded a culture of B. coli and pathological report of chronic inflammation. In case 4 incision and drainage of the space of Retzius was performed and necrotic material excised from the symphysis pubis. The pathologist reported "fragments of cartilage and fibrous tissue with nonspecific inflammation."

In January 1946, a colleague referred to me a man upon whom he had performed a two-stage suprapubic prostatectomy. He developed severe osteitis pubis with a chronic granulating sinus tract leading down behind the symphysis pubis, duration 5 months. At operation the bladder urine and wound cultures showed B. proteus. The excised sinus tract and cartilage and bone were reported chronic inflammation and necrosis.

It is therefore evident that the process is a nonspecific infection of low grade virulence.

DR. ABRAHAM HYMAN (New York, N. Y.): This is not a discussion on the various forms of prostatectomy, although I think my good friend Dr. McCarthy first called attention to the new technique for controlling hemorrhage after prostatectomy. Since this is not a discussion on prostatectomy, I will just mention it in passing.

As Dr. Aschner pointed out, the first description of osteitis or periosteitis pubis was published by Dr. Beer and I distinctly remember the first case that was diagnosed because it was rather classical. The older members who knew Dr. Beer appreciate what a fine clinician and student he was. Now here was a condition that probably had gone unrecognized for some time. We were making rounds one morning on the service when we came to the bed of a patient who had been prostatectomized about 10 or 12 days previously. The house surgeon had told Dr. Beer that the patient was complaining of rather severe suprapubic discomfort, especially on moving his lower extremities. While this description was going on by the house surgeon, Dr. Beer stood this way [indicating] with his hands on the bed and shook the bed, inadvertently. The patient complained of terrific pain in the suprapubic region. Then Dr. Beer examined him carefully and found the typical symptoms of severe pain on abduction, and tenderness over the symphysis; and that was the first description of periosteitis pubis.

There was mention this morning by the gentleman from Australia and the following speaker of the cases reported in the literature and then a vote was cast by the men here, to determine the incidence of periosteitis or osteitis pubis. They were asked to signify by raising their hands if they had had such cases. I was not amazed at the number of hands that were raised because I think one does not get any idea of the frequency of this complication by the reports in the literature. Many solitary instances are not published. We rather lost interest in this complication after Dr. Beer's first paper, although subsequently he published two or three articles.

We have had at Mount Sinai Hospital, since the last paper was published, at least eight or ten cases of periosteitis or osteitis pubis, which were not reported. I am sure many men in this audience have, on occasion, had a case or two which were not reported.

When the retropubic operation came into favor, I tried it out at the hospital on a small series of cases. We did not have a case of periosteitis pubis, but the operation did not appeal to me as a good surgical procedure and I said at the time, "This operation would never have been attempted in the days before the antibiotics," and I think subsequent reports have borne this out by the frequency of osteitis pubis.

I am not saying that you can not experience this complication in other types of suprapubic surgery. The new technique Dr. McCarthy had reference to was the control of hemorrhage by the introduction of a resectoscope transurethrally after the suprapubic enucleation; disregarding the venous bleeding but coagulating the arterial bleeders. Taking up his suggestion about 18 months ago, my colleagues and I have carried out this procedure in about seventy-five cases, and have been very well satisfied with the results. After the prostate is enucleated, the arterial bleeders should be immediately controlled by transurethral resection. A bag with a very moderate amount of inflation is introduced into the fossa and the bladder is closed primarily. I would say that 90 per cent of these patients are voiding, with the bladder completely closed in about six to eight days after operation. So far there has not been a case of osteitis pubis.

DR. FRANK C. HAMM (Brooklyn, N. Y.): The clinical picture of osteitis pubis is that of a low-grade infection. The typical symptoms, such as a long period of incubation, elevated leukocyte count, moderate anemia, mild fever, and general debility, all point to an infection of low virulence. A biopsy specimen of the pubis during the acute phase of the condition was obtained in three instances, under strict asepsis; when cultured, all specimens showed Pseudomonas aeruginosa which, in one case, was combined with B. proteus. Microscopic sections of bone disclosed an inflammatory reaction. In the literature, the presence of these organisms, in cultures from urine and from the purulent material in retropubic abscesses, has been reported but we have been unable to discover any mention of these findings in material obtained by biopsy of the symphysis. In general, this group of organisms is composed of gram-negative rod-shaped motile bodies which characteristically produce a blue-green water-soluble pigment which diffuses through the medium. They are encapsulated and form no spores. About 30 varying strains have been described, most of which are nonpathogenic. Only the Pseudomonas aeruginosa is pathogenic for man, and then only to a low degree. The organisms are found in the human intestine and on the skin. They have been isolated from water and sewage. They may produce local suppurative lesions such as wound infections, otitis media, infectious joints and in the eyes, keratitis and corneal ulcers, meningitis and possibly, a dysentery type of enteritis. Lesions produced by these organisms are refractory to treatment. None of the antibiotics, in current use, are effectual against them. Therefore, the infection must be prevented. The most obvious source of contamination seems to be the patient's skin, particularly that of the lower abdomen, genitalia and perineum. Most of the cases of osteitis pubis that I have observed, have occurred on the wards. I have seen only one case among my private patients. No cases have been discovered during a 19-month period since certain changes in our management of operative cases have been in use, namely: 1) soapy bath the night before operation; 2) further cleansing of the operative area by scrubbing for 5 minutes after the patient is placed on the operating table; 3) at operation strictly sterile precautions are observed, no exposure of the genitals and the introduction of catheters, hemostatic bags etc. are eliminated. No supporting finger is used in the rectum as a possible source of contamination.

In brief this is a plea for a meticulous atraumatic technique and asepsis second to no other branch of surgery.

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ANTIHISTAMINE—A POSSIBLE RELATIONSHIP TO OTHER FACTORS INFLUENCING INFECTION

WILLIAM P. HERBST

So-called resistance is a most indefinite thing insofar as people in general and we, the medical profession, consider it. The layman appreciates the fact that exhaustion, chilling and excessive worry or mental shock are factors which they can understand as a result of their own experience and observation. Hot foot baths, forcing fluids, hot drinks, lots of bedclothes to produce perspiration, is their practical and rather effective treatment to prevent pneumonia and acute respiratory episodes. What factors do we recognize?

Number one is usually the hemogram; if the hemoglobin and red blood count are up and the differential leukocyte count is normal, the individual is considered to have normal resistance. This is far from the fact. Metabolism in all its complexities now assumes an infinitely greater role in so-called resistance factors. The vitamin and endocrine balance along with enzyme chemical systems are the more important chemical factors for our consideration.

Homely observations in vitamin administration demonstrate that the stress and high pressure performance of the human today are greatly supported by alphabetical vitamin supplementation in their daily nutritional program and that failure to maintain such a regimen results in a state of conscious physical and mental exhaustion.

Insofar as the endocrines are concerned, there are spectacular responses in the form of rapid relief of physical and mental depression and exhaustion following the administration of androgens, estrogens, adrenal steroids, pituitary preparations and thyroid singly and in different combinations and doses. Recent clinical experience with ACTH and cortisone have accomplished such unbelievable effects as producing tissue changes which up to this time have been considered irreversible, in addition to almost instantly rendering acute and profoundly severe bacterial clinical inflammatory entities afebrile and noninflammatory. Inflammation per se assumes a most important place in most of our medical problems. It is in regard to inflammation that our resistance factors assume importance and it is in regard to inflammation that recent observations upon the action of antihistaminics are reported.

As background for observation in this presentation, two reports prompted administration of antihistamine in these patients. Kindall and Nickels reported their experience with allergic inflammatory reaction in urethral and bladder mucosa. Judd and Henderson reported improvement in cases of exudative pulmonary tuberculosis following daily administration of antihistamine drugs for a considerable time.

CASE REPORTS

Case 1. A patient who had had a nephrectomy 3 years ago presented himself with right epididymitis and orchitis of a probable acidfast origin. He had been

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Read at annual meeting, American Urological Association, Washington, D. C., June 1, 1950.

on dihydrostreptomycin and moogrol and was doing moderately well. Pyribenzamine was added to this therapy (50 mg. three times a day) and it was believed that the addition of the pyribenzamine beneficially influenced the clinical course.

Case 2. We were confronted with a situation of progressively unfavorable convalescence in a patient who had had a suprapubic prostatectomy and left ureteral lithotomy 7 days previously during which time B complex and vitamin C, penicillin and streptomycin had been continuously given. The patient continuously and progressively had more severe pain in the entire operative field and the granulations were of a dark, dusky red color instead of a bright healthy appearance. He also had a lymphedematous-like involvement of the area involving the right lower quadrant, right inguinal and femoral areas and had a deep boring pain in the right lower quadrant, with psoas spasm. The temperature recordings varied from 100 to 102.4. Pyribenzamine was given 3 times a day. Within 24 hours appreciable improvement had occurred and in 48 hours he was physically comfortable and from then on convalesced satisfactorily until he left the hospital on the fourteenth postoperative day.

After returning home he was comfortable for 3 days, but then began to have marked frequency, dysuria and pyuria for which he was given mandelamine and chloromycetin. He did not respond satisfactorily to that routine so in 3 days benedryl was added to his routine (25 mg. twice a day). In 2 days the pyuria was markedly diminished and he was again comfortable. The mandelamine and chloromycetin were then stopped and benedryl and B complex were given continuously for 3 weeks. At the end of 3 weeks the benedryl was discontinued, and after a 3-month follow-up he still remains entirely comfortable and pus-free.

Following these experiences, 7 additional patients with acute inflammatory lesions involving the urethra, the bladder and the upper urinary tract have been treated with combinations of antihistamines and chemotherapy, antibiotics and metabolic support in several combinations. Although it is impossible to determine how much the clinical course of these patients has been influenced by antihistamines, it has been the impression that they have been helpful in all except one instance, to various degrees. One patient was definitely made uncomfortable and worse when pyribenzamine was given. One patient with grade 3 pus in his prostatic secretion was rendered pus-free in a period of one week.

DISCUSSION

Several of many contributions in the literature seem to be of interest in this discussion. Menkin found that inflammations due to action of chemical or physical influences have pointed to the importance of certain amines, other than histamine, and of substances such as leukotaxine, pyrexin and necrosin. Duran-Reynals observed that various inflammatory processes produced by strongly invasive micro-organisms have been associated with the release from these organisms of a specific enzyme, hyaluronidase. Rich and Lewis observed that the tissues of an animal might become inflamed and undergo necrosis as a result of an allergic reaction following contact with tuberculo-protein. Mayer and Kull demonstrate that hyaluronidase increases the intensity of allergic skin inflammation of the epidermal type and that antihistamine substances counteract this effect. Carson and Campbell, of the Army Medical Department of Research and Graduate School, Washington, D. C., reported observations on the destructive effect of three antihistaminic compounds on fungi which are pathogenic for man.

There are many more contributions related to inflammation and invasional properties of infection of which time will not allow discussion.

Now, back to resistance; that is, resistance to infection and shock, many surgeons routinely administer polyvitamins, chemotherapeutic agents and or antibiotics before and following surgery. We routinely give penicillin and streptomycin along with B complex and vitamin C or water soluble A–B complex and C. In the light of recent ACTH effect on acute infectious inflammatory entities, the advisability of preoperatively appraising a patient's potential resistance to surgical shock and inflammation by observing the eosinophile reaction to administration of ephedrine or adrenalin may seem advisable in order to definitely indicate the degree of adrenal sufficiency or insufficiency.

In conclusion, observation of the effect of antihistamine administration in acute infectious inflammatory lesions and the metabolic mechanisms involving the inter-relationship of amines, antihistamines, enzymes, vitamins and endocrines, indicates that we have another useful and sometimes spectacular therapeutic modality available which merits further investigation in the complex and little understood field of resistance and shock mechanisms.

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REFERENCES

Carson, L. E. and Campbell, C. C.: The inhibitory effect of three antihistaminic compounds on growth of fungi pathogenic for man. Presented in Scientific Program, American Federation for Clinical Research. District of Columbia Chapter at Mt. Alto, May 19, 1950.

Duran-Reynals, F.: Tissue permeability and spreading factors in infection; contribution to host: Parasite problem. Bact. Rev., 6: 197, 1942.

Judd, A. R. and Henderson, A. R.: Use of antihistaminic drugs in human tuberculosis: A preliminary report. Ann. Allergy, 7: 306, 1949.

Kindall, L. and Nickels, T. T.: Allergy of the pelvic urinary tract in the female: A preliminary report. J. Urol., 61: 222, 1949.

Mayer, R. L. and Kull, F. C.: Influence of pyribenzamine and antistine upon action of hyaluronidase. Proc. Soc. Exp. Biol. & Med., 66: 392, 1947.

Rich, A. R. and Lewis M. R.: The nature of allergy in tuberculosis as revealed by tissue culture studies. Bull. Johns Hopkins Hosp., 50: 115, 1932.

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THE MALE FACTOR IN FERTILITY AND INFERTILITY. II. SPERMATOZOÖN COUNTS IN 1000 MEN OF KNOWN FERTILITY AND IN 1000 CASES OF INFERTILE MARRIAGE

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This paper is the second in a series designed to analyze every aspect of semen quality in terms of the fertility of the donor. The primary aims of this work are:

1) To study the characteristics of semen from fertile men and to compare them with those from men whose wives have difficulty in conceiving.

2) To determine with as much precision as statistical analysis will allow the lowest semen standards compatible with relative ease of conception.

3) To determine the optimal conditions which permit production of semen of the quality defined in No. 2.

4) To relate semen quality to the medical history of the individual.

The conditions of this study are presented in detail in the first paper of this series which dealt with ejaculate volume.[1] It was shown that the mean ejaculate volume for 800 men of known fertility was 3.33 cc in contrast to that of 3.59 cc for 600 men in "infertile" marriage. The "infertile" mean was significantly higher, the difference being due, in great part, to the "infertile" men whose semen quality was poorest.

We now have completed the analysis of 1000 men in each group (fertile and "infertile"). Before passing to discussion of the sperm counts in these individuals, we believe it appropriate to present a brief summary of the volume figures for 1000 fertile and 1000 "infertile" men. These figures are presented in detail in figure 1 which shows the relative frequency distributions of semen volume. As would be expected, these distributions are quite similar to those presented previously for smaller groups. The mean volume for 1000 (not shown in fig. 1) fertile men is 3.4 cc. (S. D.* = 1.9) and 3.7 cc (S. D. = 1.7) for 1000 "infertile" men. The difference is significant. As in the previous analysis, the highest ejaculate volumes in the "infertile" group are associated with the poorest semen specimens as measured by sperm counts. We shall discuss this relationship later in detail.

SPERMATOZOAN COUNTS IN FERTILE AND "INFERTILE" MARRIAGE

The relationship of the spermatozoan count to fertility has been a much-debated point for many years. The work of Meaker[2] and Macomber and Saunders[3] in which the figure of 60,000,000/cc was given as the lowest sperm count level compatible with fertility has been accepted generally by workers in the

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This work has been done under a research grant to the senior author by C. V. Whitney, to whom grateful acknowledgement is made.

Azoospermias are not included in these initial studies. They will be studied later as a special group.

* S.D. = Standard Deviation.

[1] MacLeod, J.: J. Fert. & Steril., 1: 347, 1950.

[2] Meaker, S. R.: Human Sterility. Baltimore: Willaims & Williams Co., 1937.

[3] Macomber, D. and Saunders, N. B.: New England J. Med. 200: 981, 1929.

field. However, it has been obvious to many that this figure is too high. Hotchkiss et al.[4] in a study on 200 fertile men found 25 per cent of his cases below the 60,000,000/cc level and Kaufman[5] in a series of 100 similar cases found 15 per cent below this level. The lowest count/cc level found by Farris[6] in 49 fertile men was 50 million/cc and he has gone further[7] in claiming that the total number of active spermatozoa is a more reliable measure of fertility than count/cc. His claims will be discussed below.

A study of the literature makes it clear that standards of male fertility are based on inadequate sampling of populations. For example, it would seem appropriate to base these standards on semen quality in fertile men who never had a sterility problem. Such men are never seen by doctors or clinics. The only such studies in the literature are those of Hotchkiss et al.[4] and Kaufman[5] in which groups of 200 and 100 men respectively were examined. These numbers are very small when compared to the large samples of "infertile" men whose semen quality has been analysed. Actually, standards of semen quality are based on so-called defects which have been found in the semen of "infertile" men with little knowledge of the prevalence of such defects in "normal" men. The following analysis is based on semen quality in 1000 men whose wives were pregnant at the time the semen was examined. The wives were passing through the antepartum clinic of The Lying-in-Hospital. Only a very small percentage of this group had sterility problems prior to their pregnancy. In most cases, conception

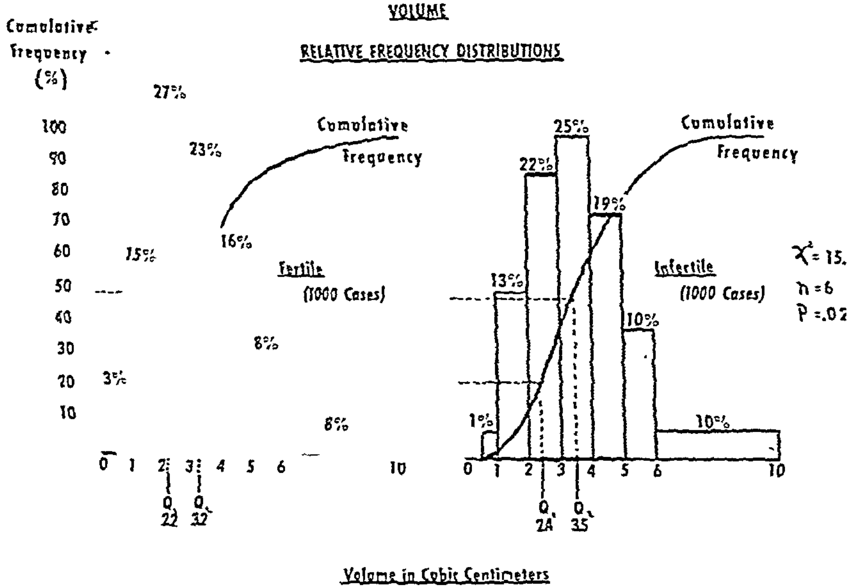

FIG. I

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[4] Hotchkiss, R. S., Brunner, E. K., and Grenley, P.: Am. J. M. Sc., 196: 362, 1938.
[5] Falk, H. C. and Kaufman, S. A.: J. Fert. & Steril., 1: 489, 1950.
[6] Farris, E. J.: J. Urol. 61: 1099, 1949.
[7] Farris, E. J.: J. Urol. 58: 85, 1947.

took place either inadvertently (20 per cent) (in spite of contraception) or within 6 months (55 per cent). A parallel study of semen quality in 1000 cases of infertile marriage was carried on simultaneously. This group comprised couples whose period of infertility ranged from a few months to 15 years. In certain instances the infertility problem involved repeated miscarriage, still-births and "one-child" sterility. These cases will be analysed separately.

RELATIVE FREQUENCY DISTRIBUTIONS OF SPERM COUNTS IN FERTILE AND INFERTILE MARRIAGE

The most valuable information as to the differences between the fertile and "infertile" men can be gained from an analysis of the relative frequency distributions of the sperm counts in both groups. The distributions for the sperm counts/cc are shown in figure 2 and as one would expect, the groups differ significantly from each other. The main points of difference are most instructive and can be summarized as follows:

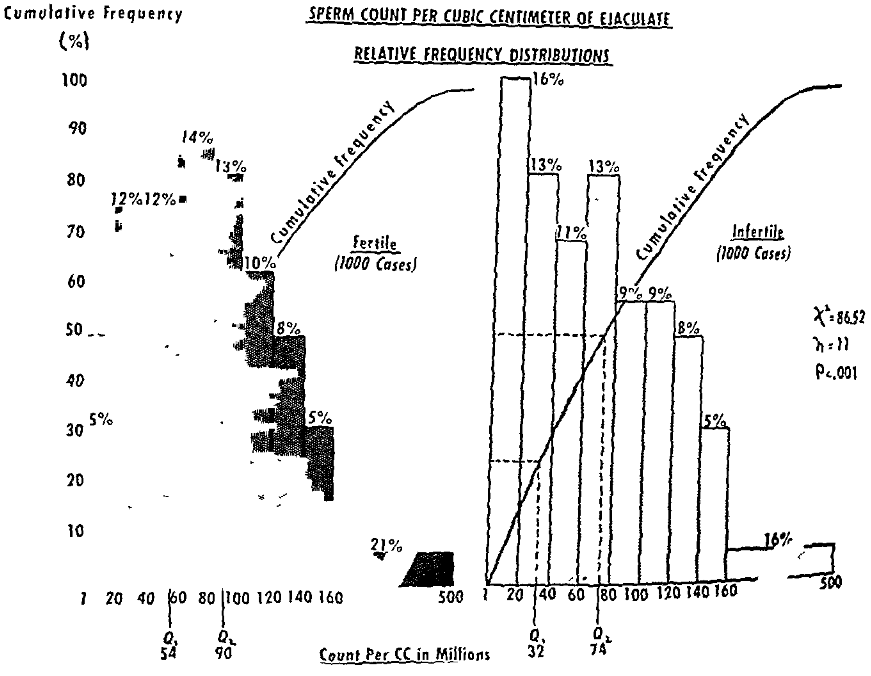

FIG. 2

a) The greatest contrast between the two groups is seen at the count levels under 20 million/cc. Only 5 per cent of the fertile men compared with 16 per cent of the "infertile" group fall in this category (9 per cent of the "infertile" men had counts under 10 million/cc whereas only 2 per cent of the fertile men are at this low level).

b) The peak for the "infertile" group is under 20 million/cc while the modal count class for the fertile group is 60–80 million/cc (using classes of 10 units width instead of 20, the modal groups are under 10 million/cc for the infertile group and 70–80 million/cc for the fertile men).

c) Fifty per cent of the "infertile" men (indicated by Q_2 on the figure) had counts of 74 million/cc or less whereas half of the fertile men are over 90 million/cc. One-fourth (Q_1 in figure) of the "infertile" group had counts under 32 million/cc while 25 per cent of the fertile men had counts up to 54 million/cc (29 per cent of the fertile men had counts under 60 million/cc).

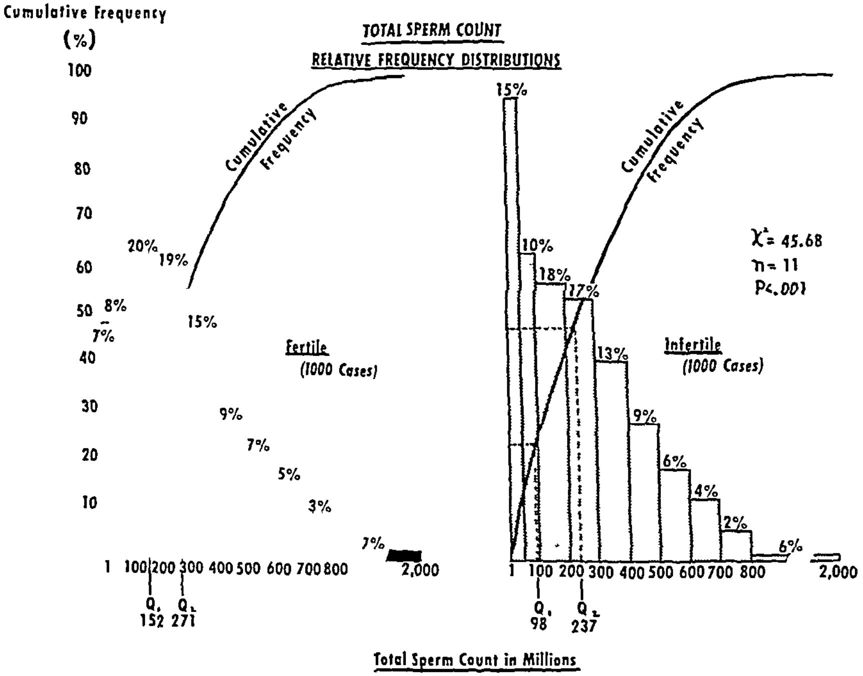

FIG. 3

d) Arithmetic means also are significantly different. The mean (average) count for 1000 fertile men is 107 million/cc. (S. D. 74 million/cc) and 90 million/cc (S. D. 76 million/cc for 1000 "infertile" men. But as we have pointed out previously,[8] averages do not represent the true differences between the groups and, indeed, can be most misleading. For example, the average of 90 million/cc for the "infertile" group could be construed as representative of the "infertile" group which it most certainly is not. We present these "average" figures merely as a basis of comparison with similar figures given by other workers in the field.

TOTAL SPERM COUNTS IN FERTILE AND INFERTILE GROUPS

It is a matter of debate as to whether sperm counts /cc or the total number of spermatozoa in the ejaculate is the more important factor in semen quality.

[8] MacLeod, J: J. Fert. & Steril., 2: 115, 1951.

We shall discuss this point in detail later and present now the frequency distributions of the total sperm counts in both groups. These are presented in figure 3. The main points can be summarized briefly. As in the counts /cc the greatest difference between the two groups lies in the "low total count" levels. Where only 7 per cent of the fertile men had total counts under 50 million 15 per cent of the "infertile" men fall in this category. The remaining distributions in both groups compare well with each other. We present the average total counts for what they are worth. The average total count for the fertile group is 350 million (S. D. = 295 million) compared to 308 million (S. D. = 282 million) for the "infertile" group. While the difference between the two figures is small it is significant but the significance is meaningless if averages alone are considered.

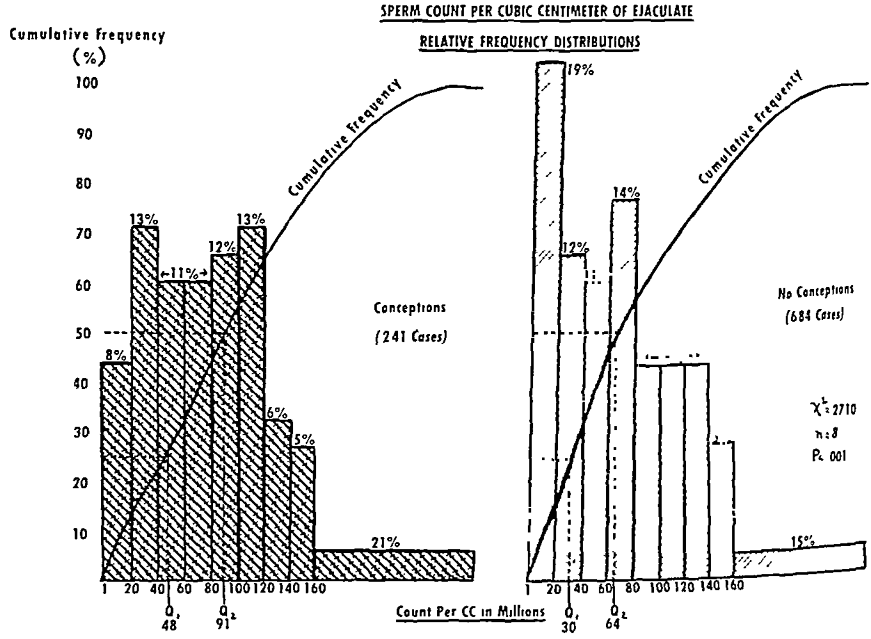

FIG. 4

ANALYSIS OF SPERM COUNTS IN FERTILE AND INFERTILE GROUPS

So far we have considered all the men in the infertile marriage group as "infertile" but it is obvious that, in a large percentage of these cases, the fault is on the female side and that the fertility of the husbands in such instances may be good. We shall consider this point in more detail later in another paper. Similarly, as we have pointed out above, many cases of infertile marriage can be classified under the headings of repeated miscarriage, still-birth, "one-child" sterility. If we take conception *only* as the end-point in male fertility without considering *at this time* semen quality as a factor in miscarriage and other abnormalities of pregnancy, we can subdivide the "infertile marriage" group solely on the basis of conception performance. In our group of 1000 "infertile" men, 241 have produced one or more conceptions *prior* to the semen examination either in the same marriage or in a previous marriage. Six hundred and eighty-four never had produced conception prior to the semen examination. In the remaining 75 cases the history is incomplete. When the sperm counts of the two groups are analyzed, valuable evidence corroborative of the data in figures 2 and 3 is obtained. Figure 4 gives the relative frequency distributions of sperm counts/cc of the "conception" and "no conception" groups of the "infertile marriage" group. The two distributions bear the same relationship to each other as the original fertile and "infertile" marriage groups. The most striking feature is that the frequency distribution of counts in the "conception" group virtually is the same as that of the fertile marriage group. In other words, if we were forced to use as fertility standards only the counts of men in the "infertile marriage" group who had produced conception, the results would be similar.

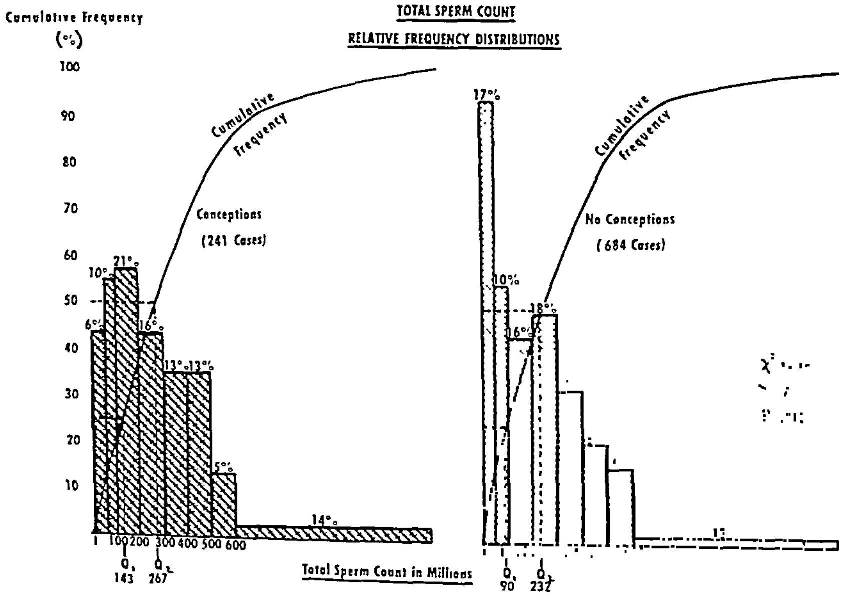

FIG. 5

Breaking down the data in fig. 4, only 8 per cent of the "conception" group fall under 20 million/cc as compared to 19 per cent in the "no conception" group. (Only 3 per cent of the "conception" group fall under 10 million/cc in contrast to 11 per cent in the "no conception" group.) As in the fertile and "infertile" marriage groups, the greatest contrast in the frequency distributions lies in the "under 20 million" class.

The "total count" distributions (fig. 5) require little comment. Again, the similarity between the "conception" and the fertility groups is striking. As in the fertile and "infertile" groups, the greatest difference is found at the lowest "total count" levels (under 50 million).

A STANDARD FOR FERTILITY BASED ONLY ON SPERM COUNTS

We have suggested that a count of 60 million/cc as a minimal standard for normal fertility is too high, and have shown (fig. 2) that nearly 30 per cent of our fertile men are under the 60 million/cc level. This large number cannot be ignored. Careful re-examination of the data presented here shows rather precisely that the minimal standard for male fertility is much lower than 60 million/cc if we take sperm count as the only criterion of fertility. We realize that other factors (motility, morphology) must be considered, but on the basis of count alone certain valuable information is obtained by an extension of the analysis already presented.

If we consider only fertile men it is obvious (fig. 2) that we cannot propose a minimum standard which would include *all* the fertile men represented in our data since of necessity such a standard would have to include all the men in the "infertile" marriage group as well. However, we may set the minimum standard at the count level above which 95 per cent of the fertile men are found. To be sure, this figure is arbitrary but it is often used in such analyses and disregards few (5 per cent) of the fertile group observations as due in some manner to "chance." This procedure would place the minimum standard at about 20 million/cc.

A more precise approach to this problem is shown in table 1. The first section (group 1) represents the 1000 fertile and 1000 "infertile" marriage cases, a total of 2000 semen specimens. If we classify these 2000 observations according to sperm count/cc, we obtain the figures in the first column. Thus, a total of 211 men from both groups had counts under 20 million/cc and 248 were between 20–39 million/cc, etc. We emphasize that 1000 (50 per cent) of the cases are contributed by the "fertile marriage" group. If count/cc were *not* a discriminating factor in fertility, one would expect the number of cases falling in each count classification to be evenly distributed as to "fertility" or "infertility." This is not the case as is shown by examination of the proportion contributed by the fertile group to each count level (column 2, table 1). Thus, the fertile marriage group contributed only 22 per cent to the 211 cases under 20 million/cc whereas on the basis of independence of fertility and sperm count this group should have contributed 50 per cent (a highly significant difference). At the 20–39 million/cc count level this proportion jumps dramatically to 47 per cent not significantly less than 50 per cent. (It should be emphasised that advancing in 10 million/cc units gives the same result—the big jump occurs at 20 million/cc.) The only count levels to which the fertile group contributes significantly more than 50 per cent are 80–99 and 160 million and over /cc. But we do not believe that these points have any practical significance inasmuch as the proportion contributed by the fertile group to counts of 20 million/cc and over would have to be greater than 50 per cent to make up for the deficiency under this level. Along this line of thought, another interesting fact shown by the data in table 1, column 2 is that the proportion contributed by the fertile group at each count level does *not* rise consistently as might be expected if fertility were consistently proportional to count levels. In other words, the figures strongly suggest that *on the basis of sperm count alone* a semen specimen with a count of 140 million/cc does not have a higher fertility potential than one of 40 million/cc. But we should make clear that the figures are not to be construed as probabilities of fertility. The contribution of 22 per cent by the fertile group to the "under 20 million/cc" class is *not* the probability that a man with such a count is fertile. This figure depends on the equal sampling of the fertile and "infertile" groups, but the pattern would be similar whatever the ratio of sample sizes to each other.

TABLE 1

COUNT PER CUBIC CENTIMETER IN MILLIONS	GROUP I (2000 CASES)			GROUP II (925 CASES)			GROUP III (925 CASES)		
	A. Fertile Marriage (1000 Cases) B. Infertile Marriage (1000 Cases)			A. Men in infertile marriage with history of conception(s) prior to semen exam (241 Cases) B. Men in infertile marriage with history of no conception prior to semen exam (684 Cases)			A. Men in infertile marriage with conception(s) prior to *or* after semen exam (319 Cases) B. Men in infertile marriage with no conception prior to or after semen exam (606 Cases)		
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)
	No. of Cases in Count Class	Proportion Contributed by A	Difference from 50.0%	No. of Cases in Count Class	Proportion Contributed by A	Difference from 26.1%	No. of Cases in Count Class	Proportion Contributed by A	Difference from 34.5%
All Cases	2000	50.0%	—	925	26.1%	—	925	34.5%	—
Under 20	211	21.8%	Signif.	152	13.2%	Signif.	152	19.1%	Signif.
20–39	248	47.1%	Not Sig.	118	26.3%	Not Sig.	118	37.3%	Not Sig.
40–59	237	52.7%	Not Sig.	104	26.0%	Not Sig.	104	30.8%	Not Sig.
60–79	271	52.4%	Not Sig.	120	21.7%	Not Sig.	120	35.0%	Not Sig.
80–99	220	59.1%	Signif.	81	34.6%	Not Sig.	81	43.2%	Not Sig.
100–119	191	49.7%	Not Sig.	83	37.3%	Mod. Sig.	83	44.6%	Mod. Sig.
120–139	157	52.2%	Not Sig.	69	20.3%	Not Sig.	69	30.4%	Not Sig.
140–159	96	52.1%	Not Sig.	45	28.9%	Not Sig.	45	37.8%	Not Sig.
160–Over	369	57.7%	Signif.	153	33.3%	Mod. Sig.	153	40.5%	Not Sig.

Significant—probability less than .01.
Mod. Sig.—probability between .01 and .05.
Not Sig.—probability greater than .05.

These points are given greater weight if we now consider more carefully only the "infertile" group and the proportion or cases at each count level in which the husband already had produced a conception (group 2). The "20 million/cc" mark (column 5) again is outstanding. Here, 241 out of 925 cases (26 per cent) had a history of one or more conceptions prior to the semen exam. Reasoning as before, we may expect 26 per cent of the cases at all count levels to come from the conception group. The count level under 20 million/cc again is significantly deficient, only 13 per cent of the cases being contributed by the "conception" group. As before, immediately above this level (20–39 million/cc) the expected proportion is reached.

Of the remaining 684 men in the "infertile" group with no prior conceptions, conception has resulted in 78 of these cases since the semen examination (25 conceptions have since been reported by the cases with previous conceptions). When we add the 78 new conception cases to the old group of 241 we get a total of 319 men known to have produced a conception at some time. The analysis of this group of 319 is shown in group 3 of table 1 and leads to the same conclusions as those reached for groups 1 and 2, namely, that the "under 20 million/cc level" is the highly significant point of demarcation for fertility if only count/cc is used as the criterion of fertility.

We have performed a similar analysis for total sperm counts in all 3 groups (table 2). In all groups, the only count level at which significantly fewer cases are contributed by the fertile and "conception" groups is under 50 million. Above that count level, no significant differences from the expected proportions are found. As in the case of count /cc the proportions do not rise with rising count level.

TABLE 2

TOTAL COUNT IN MILLIONS	GROUP I (2000 CASES)			GROUP II (925 CASES)			GROUP III (925 CASES)		
	A. Fertile Marriage (1000 Cases) B. Infertile Marriage (1000 Cases)			A. Men in infertile marriage with history of conception(s) prior to semen exam (241 Cases) B. Men in infertile marriage with history of no conception prior to semen exam (684 Cases)			A. Men in infertile marriage with conception(s) prior to *or* after semen exam (319 Cases) B. Men in infertile marriage with no conception prior to or after semen exam (606 Cases)		
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)
	No. of Cases in Count Class	Proportion Contributed by A	Difference from 50.0%	No. of Cases in Count Class	Proportion Contributed by A	Difference from 26.1%	No. of Cases in Count Class	Proportion Contributed by A	Difference from 34.5%
All Cases	2000	50.0%	—	925	26.1%	—	925	34.5%	—
Under 50	214	29.9%	Signif.	136	14.0%	Signif.	136	21.3%	Signif.
50–99	186	44.6%	Not Sig.	95	26.3%	Not Sig.	95	33.7%	Not Sig.
100–199	381	53.8%	Not Sig.	161	31.1%	Not Sig.	161	40.4%	Not Sig.
200–299	362	53.6%	Not Sig.	157	23.6%	Not Sig.	157	29.9%	Not Sig.
300–399	277	53.1%	Not Sig.	114	28.1%	Not Sig.	114	41.2%	Not Sig.
400–499	178	50.6%	Not Sig.	86	36.0%	Not Sig.	86	43.0%	Not Sig.
500–599	126	53.2%	Not Sig.	54	22.2%	Not Sig.	54	35.2%	Not Sig.
600–Over	276	54.3%	Not Sig.	122	28.7%	Not Sig.	122	35.2%	Not Sig.

Significant—probability less than .01.
Not Sig.—probability greater than .05.

THE RELATIONSHIP OF EJACULATE VOLUME TO SPERMATOZOAN COUNTS

As part of this protracted analysis of semen quality in fertility and infertility, it is essential that as each aspect of semen quality is analyzed, its relationship to the other qualities be determined. Our analysis of ejaculate volume is on record[1] and now we have presented data on sperm counts. It remains for us to show the relationship between volume and sperm counts in fertile and "infertile" men.

For this purpose, it is necessary to divide the volume and count /cc into classes so that comparisons can be made between each quality in each class. We have chosen the following as our class limits in each quality:

Volume	Count/cc
Under 2.4 cc	Under 40 million
2.4–3.3 cc	40–79 million
3.4–4.4 cc	80–139 million
4.5 cc and over	140 million and over

We have not selected these classes arbitrarily but rather because they correspond roughly to the quartiles represented in figures 1 and 2 for volume and counts/cc respectively.

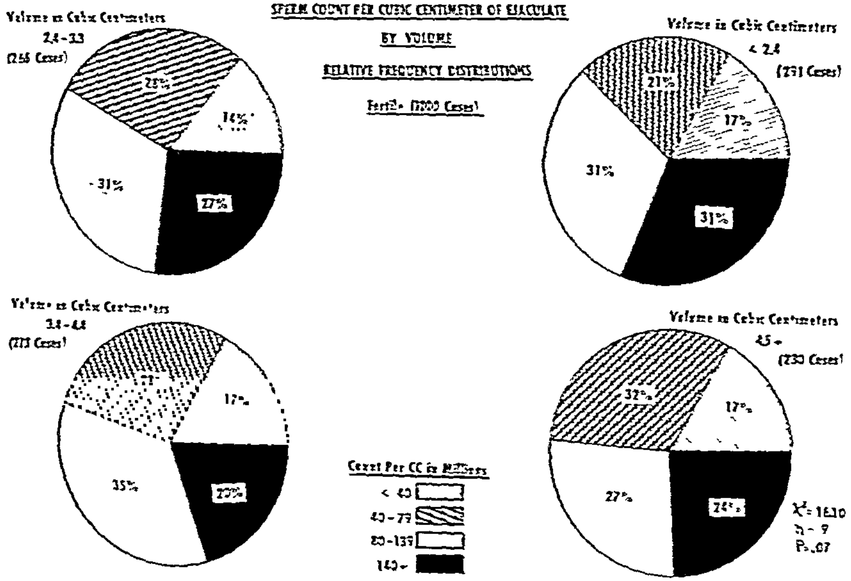

FIG. 6

If we take the 1000 cases in the "fertile" group, figure 6 shows that there is no significant relationship between ejaculate volume and sperm counts/cc. In contrast, there is a highly significant relationship between volume and count in the 1000 "infertile" cases (fig. 7). In this group, as volume increases, the proportion of low counts increases and the proportion of high counts decrease. In the 40–79 million/cc count level, the proportions remain relatively constant. This difference between semen quality in the "fertile" and "infertile" groups delineates more sharply what we already have demonstrated, namely, that the higher volumes are associated with the poorer sperm counts in the "infertile" group. We have carried this analysis further and considered the volume-count relationship in the "conception" and "no-conception" groups of the "infertile marriage" group. Because of space limitations we can state quite briefly that there is no significant relationship between volume and count in the "conception" group whereas in the "no-conception" group there is the same type of relationship as in the "infertile marriage" group.

This discussion of volume-count relationship cannot be concluded without

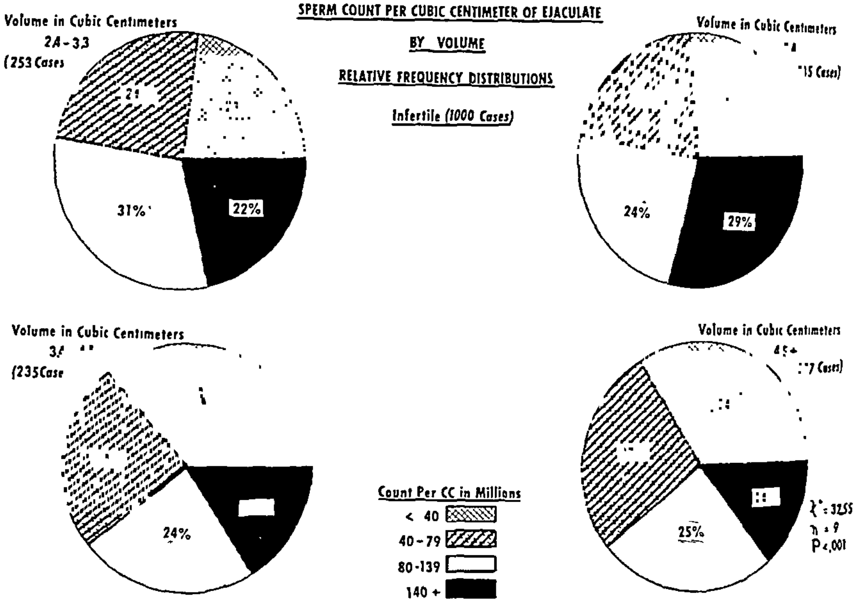

Fig. 7

TABLE 3

COUNT PER CC IN MILLIONS	COMPARISON WITHIN VOLUME CLASSES OF COUNT PER CC DISTRIBUTIONS							
	Volume under 2 4 cc		Volume 2.4 cc–3.3 cc		Volume 3.4 cc–4.4 cc		Volume 4 5 cc and over	
	Proportion of Cases		Proportion of Cases		Proportion of Cases		Proportion of Cases	
	Fertile	Infertile	Fertile	Infertile	Fertile	Infertile	Fertile	Infertile
40	17%	26%	14%	23%	17%	36%	17%	34%
40–79	21%	21%	28%	24%	28%	24%	32%	27%
80–139	31%	24%	31%	31%	35%	24%	27%	25%
140+	31%	29%	27%	22%	20%	16%	24%	14%
Total	100%	100%	100%	100%	100%	100%	100%	100%
No. of Cases.	291	235	266	253	213	235	230	277
Median Count per cc.	103	88	95	86	89	64	82	63
Differences between Distributions	$\chi^2 = 7.60$, $N = 3$, $P = .05$		$\chi^2 = 6.91$ $N = 3$, $P = .07$		$\chi^2 = 21.02$, $N = 3$, $P < .001$		$\chi^2 = 21.53$, $N = 3$, $P < .001$	

reference to the data in table 3 which compares the sperm count/cc distributions between the "fertile" and "infertile" groups at all volume levels. The main points of interest in the table are 1) that, at all volume levels the counts of the "fertile" group are better, 2) for volumes under 3.4 cc, the differences in counts between the "fertile" and "infertile" groups are not significant, and 3) at volume levels of 3.4 cc or over, the difference between sperm counts in the two groups is highly significant.

DISCUSSION

We believe that this analysis indicates that a more realistic approach must be made to an estimate of human male fertility insofar as spermatozoön counts are concerned. Using only this criterion it is clear that the range of "normal" fertility in the male is much wider than was once supposed. When we have completed our presentation of similar analyses of motile activity and morphology we do not expect to modify this position. While it is certain that no man can be considered sterile as long as a single spermatozoön appears in his semen, it is clear that the chances of producing conception increase with rising sperm counts up to a certain point. Superficially, it may seem trite to make this statement. But it should be remembered that the most careful workers in the field of male infertility have, of necessity, been vague in their stand as to the point at which semen quality falls in the "infertile" class. Our aim is to clarify this position if it is possible to do so.

Two important and well-defined facts emerge from the data that we have presented. The first is that the essential difference between fertile and "infertile" groups lies at a low sperm count level. The differences between the two groups above 20 million/cc are insignificant. We interpret this to mean that it is at the 20 million/cc level that we must consider real "infertility" as beginning although we cannot preclude conception as possible below that level. If we had reached this conclusion by merely comparing groups of men whose semen produced conception easily with that of men who had difficulty, we would be justified in suggesting that semen quality standards should be lowered. But when we ignore the fertile men in our analysis and consider semen quality only in the "infertile" group, and reach the same conclusions by such a completely independent analysis, we are even more confident that the 20 million/cc count level is most significant.

The second important inference we can derive from the data is that above the critical 20 million/cc level, the chances of conception do not rise proportionally with the increase in sperm count and, in fact, do not increase significantly above this level. Farris,[6] on a scant amount of data, has made several sweeping generalizations in regard to male fertility, one of which we can discuss at this time, namely, that an individual whose semen contains less than 80 million active spermatozoa is "subfertile" (semen with from 80–185 million active spermatozoa is only "relatively fertile"). In order to meet his "relatively fertile" standards and allowing a generous "80 per cent active cells," a total spermatozoan count of from 100–200 million would be necessary according to the Farris standards. Thus, from 15 to 35 per cent of our fertile men would be "subfertile." This is considerably more than the "occasional pregnancy" allowed to this group by Farris.

In regard to the significance of sperm counts/cc as against total sperm count it seems to make little difference which point of reference is used as a standard.

The sharp difference between the fertile and "infertile" group lies at the "under 50 million total count" level.

It is of interest to compare our data with those obtained from other studies of fertile men in the literature. The work of Hotchkiss et al.[4] on 200 men of known fertility particularly is interesting when a comparison is made of the number whose sperm counts fall in the lower count levels. For example, their figure and ours for counts under 20 million/cc are identical, 5 per cent in each case. Similarly, for count levels between 20 and 40 million/cc, the figures are 10 per cent and 12 per cent respectively, again virtually the same. And at the 40–60 million/cc level, their figures are 11 per cent, ours 12 per cent.

The next largest series on fertile men is that of Falk and Kaufman.[5] Their 100 men were selected on a much more rigid basis inasmuch as they were required to have had at least two normal pregnancies (with no miscarriages) to their credit before qualifying as normal, fertile men. We have taken the first 100 semen examinations examined in our fertility group, the donors of which had a pregnancy history corresponding to the Falk and Kaufman criteria and used the data for comparison. They found fewer cases under 60 million/cc (15 per cent compared to our 22 per cent) and none of their semen specimens were under 20 million/cc (we found 4 per cent). We do not believe these differences to be a matter of concern since we have found considerable variation in the relative frequency distributions if we study our 1000 fertile men in groups of 100 in order of observation.

More recently, Page and Houlding[9] presented a most comprehensive and well-analysed study of semen quality in a group of 1000 cases applying for treatment of their infertility problem. They subdivided their series of 929 cases into classes of "fertile" and "unknown fertility" on the basis of whether or not conception took place within 6 months of the semen examination. They did not include in their analysis cases in which conception had occurred prior to the initial semen examination nor do they mention cases in which conception took place later than 6 months thereafter. For these reasons it is impossible to conduct any comparison between their data and ours at this time. We propose to postpone this analysis until we have a comparable amount of follow-up data.

Obviously, this unilateral approach to the problem of infertile marriage where only semen quality is considered, is not enough. We must consider both husband and wife and analyse semen quality further in terms of deficiencies in the wife. This analysis is in progress and will be published. Similarly, the relation of continence, frequency of intercourse, age of the individual, etc. to semen quality are being considered in this analytical fashion and the data made available as soon as possible.

SUMMARY

Data are presented on semen quality in 1000 fertile men and 1000 men in "infertile" marriage.

The median ejaculate volume for the fertile group is 3.20 cc. and 3.50 cc for the "infertile" group. The difference is significant and is discussed.

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[9] Page, E. W. and Houlding, F.: In press., J. Fert. & Steril.

The median spermatozoön counts/cc for the fertile group is 90 million and 74 million for the "infertile" group. The real difference between the two groups lies in the relative frequency distributions and only at the lower count levels, namely, below 20 million/cc.

In a similar analysis of total spermatozoön counts, the real difference between the fertile and the "infertile" groups lies at count-levels under 50 million/cc.

The relationship between ejaculate volume and spermatozoön counts is analyzed and discussed.

We are deeply indebted to Prof. R. Gordon Douglas of the Department of Obstetrics and Gynecology, Cornell Medical College, for the facilities of his department and for the wholehearted cooperation he has extended in this study.

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THE ROLE OF THE UROLOGIST IN THE PROBLEM OF INFERTILITY

ISADORE GERSH

The urologist by his training, experience, and technical facilities is logically the practitioner who should be best qualified to investigate and evaluate the condition of the reproductive system in men and to treat disorders in the male which result in disturbances in fertility. The urologist has a definite advantage over the physician who studies the woman in a barren marriage, because the seminal fluid and more particularly, the spermatozoa, may be studied, while in the female the evidence is much less direct.

Until the past two decades the wife usually bore the responsibility for her childlessness. Now, even most laymen realize that husbands are responsible at least *almost* as often as wives in sterile matings. In many cases it is impossible to place the fault entirely upon either the man or the woman, and as Meaker[1] has pointed out, "involuntary barrenness is a matter of divided responsibility in the large majority of cases." Tyler and Payne[2] analyzed a series of 65 couples referred primarily as gynecologic problems and in two-thirds of these cases they found an important male factor in the infertility problem. Keshin and Pinck[3] reported defective semen to be a factor in 68 per cent of 135 cases. Michelson and Michelson[4] in a group of 855 barren couples found 519 men with impaired fertility. Of 287 cases in which complete data on the fertility of both mates was obtained, they found that "both were apparently fertile in 99 of these cases, and the husband was either a contributing or sole cause of the childlessness in 127."

The fertility status of the male is determined after a careful history, a thorough physical examination, and certain laboratory procedures including studies of one or more seminal specimens have been obtained. Ideally the findings in the male should be available when the investigation of the wife is carried out. The details of fertility studies in the male are recorded in numerous publications, including those by Hotchkiss,[5, 6] Williams and Simmons,[7] Lane-Roberts,[8] and Weisman.[9]

Read at annual meeting, South Central Section, American Urological Association, Tulsa, Okla., September, 27, 1950.

[1] Meaker, S. R.: Male infertility from a gynecologic viewpoint. J. Urol., 43: 871–890, 1940.

[2] Tyler, E. T. and Payne, S.: Spermatogenesis and the therapy of infertility. J. A. M. A., 134: 770–774, 1947.

[3] Keshin, J. G. and Pinck, B. D.: Factors in male sterility. Am. J. Surg., 66: 346–356, 1944.

[4] Michelson, L. and Michelson, R.: Fertility studies of the male in barren marriages. J. A. M. A., 134: 941–943, 1947.

[5] Hotchkiss, R. S.: Methods in sperm analyses and evaluation of therapeutic procedures. J. A. M. A., 107: 1849–1851, 1936.

[6] Hotchkiss, R. S.: Fertility in men. A clinical study of the causes, diagnosis, and treatment of impaired fertility in men. Philadelphia: J. B. Lippincott, 1944.

[7] Williams, W. W. and Simmons, F. A.: The clinical approach to the diagnosis of sterility. Urol. & Cutan. Rev., 46: 558–570, 1942.

[8] Lane-Roberts, C., Sharman, A., Walker, K. and Wiesner, B. P.: Sterility and impaired fertility. New York: Hoeber, Inc., 1939.

[9] Weisman, A. I.: Recent advances in the clinical evaluation of spermatozoa. West. J. Surg., Obst. and Gynec., 50: 339–344, 1942.

HISTORY AND PHYSICAL EXAMINATION

The record should include all the details covered in a clinical history with emphasis on factors having any possible bearing on fertility. The history should reveal details of any previous marriages and if possible whether the divorced mate has remarried and had children. A history of gonorrhea in the male is of little value unless one learns whether there were complications, such as posterior urethral involvement and epididymitis. Nonspecific epididymitis may also account for obstruction to spermatozoal migration. A history of mumps is especially important if the disease occurred in adulthood and was complicated by orchitis. Any history of swelling or abnormality in development and descent of the testicles should be noted. Systemic diseases and infectious processes are important because they may depress spermatogenesis.

In the physical examination the urologist will note any urethral deformities or strictures and changes in size or consistency of the testes Genital abnormalities will often indicate what will later be confirmed by examination of seminal specimens. The prostate and seminal vesicles should be carefully palpated and the expressed secretions examined microscopically on one or more occasions. Other possible foci of infection should also be searched for. The development of the secondary sex characteristics and the state of the endocrine system are noted. A urinalysis, blood count, and a serologic test for syphilis are routine. Patients showing endocrine disturbances and those in whom seminal deficiencies are found, should have a basal metabolic determination.

COLLECTION AND EXAMINATION OF SEMINAL SPECIMENS

The seminal specimen is collected by masturbation or withdrawal and ejaculation into a sterile wide-mouthed bottle after an interval of 3 to 5 days since any emission has occurred. In most cases I examine a specimen collected by each method. It is important that the entire specimen of a complete ejaculation be obtained. MacLeod and Hotchkiss[10] showed that the first 40 per cent of the ejaculate contains approximately 75 per cent of the spermatozoa, and they have superior motility. In my experience faulty handling of the specimen between the time of collection and delivery to the office results not infrequently in impaired motility and survival rate of the sperm. Condom specimens are to be condemned since both the latex and the powder used in their manufacture are inimical to spermatozoa.

The specimen is examined soon after liquefaction has occurred. Seminal fluid is alkaline. Normal volume varies from 2.5 to 6.0 cc. Excessive viscosity may interfere with sperm motility. The quality of motility is an important attribute of sperm; however, as Williams[11] has pointed out, motility is a characteristic not only of normal sperm, but also of "most spermatozoa that are not fit for impregnation purposes." Survival rate is determined by examining a wet drop every few hours; at room temperature a normal specimen will still contain some motile spermatozoa after 24 hours. Opalescence of the fluid gives a rough impression of cellular concentration. Specimens with low counts are thin and watery in appearance. Highly fertile semen contains 80 million or more spermatozoa per cubic centimeter. Some authors have stressed the importance of the total count as well as the concentration per cubic centimeter, while Farris[12] places emphasis on the total number of active sperm in the entire specimen. To study the morphology, smears may be stained by several methods. The procedure of Williams[13] using crystal violet and aqueous rose bengal, in my experience, is simple and satisfactory. Moench and Holt[14] considered that fertility is impaired when abnormal forms are more than 20 per cent. I am impressed by the fact that usually as the sperm count diminishes the abnormal forms and other defects increase, as was reported by MacLeod and Hotchkiss.[15]

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[10] MacLeod, J. and Hotchkiss, R. S.: The distribution of spermatozoa and certain chemical constituents in the human ejaculate. J. Urol., 48: 225-229, 1942.

[11] Williams, W. W.: The relation of sperm motility to fertilizing ability. Urol. & Cutan. Rev., 43: 587-592, 1939.

A staining procedure recently reported by Blom[16] for differentiating live and dead (bovine) spermatozoa is based on the principle that living cells do not take up eosin. Williams and Pollak[17] applied the procedure to human semen and found that "this method which gives information about both viability and morphology, provides a valuable screening test for the average clinician." During the past few months I have used this procedure and have found it to be a helpful addition to those already in use. Spermatozoa stand out sharply against the brownish-violet background, and by this staining method it is

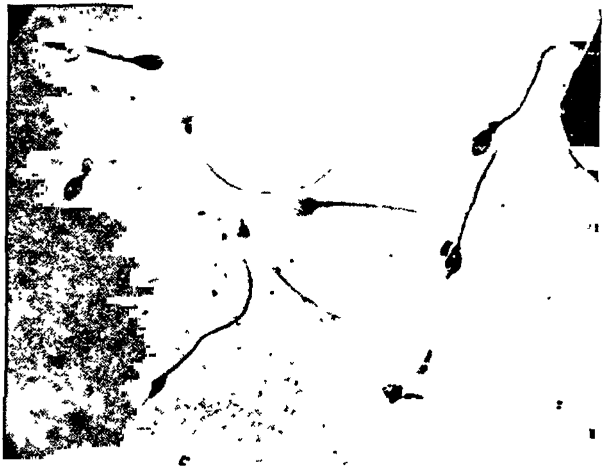

FIG. 1. Photomicrograph of eosin-nigrosin stain showing motile and nonmotile sperm; former do not take up eosin and are colorless. Note abnormal forms.

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[12] Farris, E. J.: The number of motile spermatozoa as an index of fertility in men. A study of 406 specimens. J. Urol., **61:** 1099–1104, 1949.

[13] Williams, W. W., McCugan, A. and Carpenter, H. D.: The staining and morphology of the human spermatozoon. J. Urol., **32:** 201–212, 1934.

[14] Moench, G. and Holt, H.: Sperm morphology in relation to fertility. Am. J. Obst. and Gynec., **22:** 199–210, 1931.

[15] MacLeod, J. and Hotchkiss, R. S.: Semen analysis in 1500 cases of sterile marriage. Am. J. Obst. and Gynec., **52:** 34–41, 1946.

[16] Blom, E.: A one-minute live-dead sperm stain by means of eosin-nigrosin. Fertility and Sterility, **1:** 176–177, 1950.

[17] Williams, W. W. and Pollak, O. J.: Study of sperm vitality with the aid of eosin-nigrosin stain. Fertility and Sterility, **1:** 178–181, 1950.

possible to differentiate live from dead cells as well as to obtain information about sperm morphology; see figure 1.

EVALUATION OF FACTORS IN SEMINAL STUDIES

It must be remembered that in evaluating the fertility status of a man a determination is made only of the probability of his being able to produce a pregnancy in a fertile woman. Fertility is a characteristic based on the sum of a number of factors, and pregnancy will occur only if the sum total of the male and female factors are adequate. Pregnancies will result in some cases where there are few spermatozoa and will not occur in other instances where there are an abundance of the gametes. After the man has been studied one cannot dogmatically say, unless the patient is absolutely sterile, that he will or will not eventually impregnate his wife. Hotchkiss, Brunner, and Grenley[18] found that 25 per cent of 200 men whose wives were pregnant had sperm counts below 60 million per cc., and the sperm counts were as low as 2,250,000.

In discussing male fertility in 1940, Meaker stated "the evaluation is based chiefly, though not entirely, upon the quality of the semen. To merit the rating of good, a specimen must have a sperm count above 60,000,000 per cc.; a motility of at least 70 per cent; and not more than 20 per cent of abnormal forms according to the method of my urologic associate. An intermediate specimen presents one or more of the following features: a sperm count below 60,000,000 but above 20,000,000; a motility of less than 70 but more than 20 per cent; and between 20 and 30 per cent of abnormal forms. If a specimen falls short of minimum intermediate requirements in any one of the respects, number, motility, or morphology, it is rated as poor. Thus three groups of males are defined, those of good, intermediate, and poor fertility." In the series reported below the classification of Meaker was followed with the addition of a fourth group—"sterile" —in whom no sperm were found in repeated ejaculates.

REPORT OF STUDIES OF MALE FERTILITY PROBLEMS

During a period of several years prior to World War II, I studied and treated a number of men in infertile marriages. Too often, based on published standards for male fertility, a discouraging prognosis was given, and months or years later pregnancies occurred in a number of cases in spite of semen values believed to be incompatible with fertility. As a result, during the past few years a more hopeful outlook has been expressed in these cases with seminal deficiencies.

This report deals with a review of studies in 292 white men who were referred to me from January 1946 to November 1949, for evaluation of their part in barren marriages. The necessity for cooperation between the urologist and gynecologist in these problems is obvious. In 63 cases the wives were examined by competent general practitioners and in the remainder by gynecologists. Cases were excluded from this series in which couples had been trying unsuccessfully to have a pregnancy for less than one year, those in which the mates have become divorced or separated, unmarried men who came for information regarding their fertility status before entering into marriage or who were suspected of causing a pregnancy, and those who failed to complete the necessary investigations. Follow-up information regarding pregnancies subsequent to the fertility studies was obtained in 218 couples. A larger series would be more desirable for statistical purposes; however, the figures are indicative of a trend, at least.

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[18] Hotchkiss, R. S., Brunner, E. K. and Grenley, P.: Semen analyses of two hundred fertile men. Am. J. Med. Sc., 196: 362-384, 1938.

Ages of the patients ranged from 20 to 47 years, as shown in table 1. Seventy-nine per cent (231) were married from 2 to 7 years when the study of the male factor was undertaken, table 2. Of the 292 men in the entire series (table 3), I classified 174 (59.6 per cent) as good, 52 (17.8 per cent) as intermediate, 40 (13.7 per cent) as poor, and 26 (8.9 per cent) as sterile. In the group of 218 cases with follow-up (see table 4) pregnancies occurred in 50.8 per cent of those classified as good, in 47.4 per cent of the intermediate, and in 27 per cent of the poor fertility group. No pregnancies resulted from any of the 23 men classified as sterile.

TABLE 1. *Age of 292 men in barren marriages*

Age	20–24	25–29	30–34	35–39	40–44	45–47
Number of patients .	21	112	101	46	9	3

TABLE 2. *Duration of 292 barren marriages*

Years of barren marriage	1	2–4	5–7	8–10	11–15
Number of patients	13	136	95	39	9

TABLE 3. *Fertility classification of 292 men in barren marriages*

CLASSIFICATION	NUMBER	PER CENT
Good	174	59.6
Intermediate	52	17.8
Poor	40	13.7
Sterile	26	8.9
Total	292	100.0

TABLE 4. *Follow-up studies showing incidence of pregnancies according to fertility classification of husband*

FERTILITY STATUS	NUMBER OF MEN	COUPLES IN WHICH PREGNANCY OCCURRED		NUMBER WITH PREGNANCY TO TERM	NUMBER WITH MISCARRIAGE OR TUBAL PREGNANCY	NUMBER NOW PREGNANT
		Number	Percentage			
Good .	120	61	50.8	52	6	3
Intermediate	38	18	47.4	16	2	0
Poor	37	10	27.0	7	1	2
Sterile	23	0	0	0	0	0
Total	218	89	40.8	75	9	5

There was a history of testicular swelling in 44 (15 per cent) of the 292 men, 25 having been of unilateral and 19 of bilateral involvement. Thirteen were complications of mumps, 15 were traumatic (including surgical) in origin, 10 were epididymitis caused by gonorrhea and 6 were apparently nonspecific epididymitis. On physical examination some of these patients showed no testicular abnormalities, the process having apparently resolved to a degree that changes were not recognizable by palpation. The latter were mainly patients with a history of epididymitis. Testicular changes including palpable changes in size or consistency of the testis or induration and thickening of the epididymis, were found on physical examination in 71 (24.3 per cent) of the patients in the entire series. There were, therefore, a number of men who gave no history of gonadal swelling but who nevertheless had testicles which had been involved by some disease process. Bilateral changes were sometimes found on physical examination where there was a history of only unilateral testicular involvement. It was impossible to find a cause for atrophic and hypoplastic testicular conditions in 22 cases. There were three unilateral cryptorchids and one bilateral. Culp and Benyon[19] stated in their recent report on a series of cases "that no one with a solitary normal testis had a normal sperm count."

TABLE 5. *Showing testicular findings on physical examination, fertility status from seminal studies and incidence of pregnancies in 218 cases with follow-up information*

PHYSICAL EXAMINATION	FERTILITY STATUS	NUMBER OF PATIENTS	NUMBER IN WHICH PREG. OCCURRED	PERCENTAGE WITH PREGNANCY
Normal testicles	Good	118	61	
	Intermediate	26	14	
	Poor	10	4	
	Sterile	2	0	
	Total	156	79	50.6
Unilateral testicular changes	Good	2	0	
	Intermediate	6	2	
	Poor	8	3	
	Sterile	0	0	
	Total	16	5	31.2
Bilateral testicular changes	Good	0	0	
	Intermediate	6	2	
	Poor	19	3	
	Sterile	21	0	
	Total	46	5	10.9
All cases		218	89	40.8

Of the 71 patients with testicular changes, 21 were unilateral and 50 were bilateral. Three of the latter had a combination of atrophy on one side and epididymal thickening on the other. Sixty-eight of these 71 patients, were classified as being below the "good" fertility level, and all 3 men graded as "good" had sperm counts of less than 80 million per cc. Of 218 cases with follow-up information (table 5) the wives of 79 (50.6 per cent) of the men with normal testicles on physical examination had pregnancies. Of the group with unilateral testicular changes there were pregnancies in 5 (31.2 per cent), while those with bilateral changes reported only 5 (10.9 per cent) pregnancies.

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[19] Culp, O. S. and Benyon, D. E.: Treatment of male infertility: An evaluation of medicinal therapy. J. Urol., 63: 1093–1103, 1950.

Bilateral testicular biopsies in 9 patients with seminal insufficiency were obtained and studied by the method described by Charney.[20] This is a valuable diagnostic and prognostic procedure and permits differentiation between reversible and irreversible changes in the seminiferous tubules, as well as the progress of therapy. It should be mentioned that this procedure is not always necessary for differentiation between obstructive and nonobstructive azoospermia, because stained smears in the latter cases will often reveal cells of the spermatogenic series.

TREATMENT

The treatment of the infertile and subfertile male is a challenge to the physician. The urologist is especially interested in the correction of anomalies such as hypospadias and cryptorchidism. The latter condition must be corrected before irreversible damage to the testicular tubules has occurred, as McCollum[21] has shown. He did a follow-up study on a series of cases and proved that although cryptorchidism reduced fertility, that the operated group showed definitely higher fertility. In obstructive azoospermia the urologist may be able to remove successfully the barrier or perform a shunting operation so as to bypass the obstruction in some cases. The procedure to relieve epididymal obstructions, reported by Martin[22] in 1902, in which vaso-epididymal anastomosis was performed using fine silver-wire sutures, was used by Hagner[23] in 65 cases with the result that 21 patients had numerous motile spermatozoa in their ejaculates. Humphreys and Hotchkiss[24] believe that silk is preferable to silverwire sutures for this operation.

Focal infections should be cleared up because of their general depressant effects. In some cases infection in the prostate and seminal vesicles may affect viability and motility of spermatozoa. In my series of 292 men there were 82 (28 per cent) with definitely increased leukocytes in their prostatovesicular secretions. However, disturbances in motility and survival rate of the spermatozoa could be objectively attributed to this condition in only a small proportion of the cases. The work of MacLeod[25] showing the deleterious effect of hydrogen peroxide-producing bacteria may be the explanation.

[20] Charney, C. W.: Testicular biopsy. Its value in male sterility. J. A. M. A., **115**: 1429-1443, 1940.

[21] McCollum, D. W.: Clinical study of the spermatogenesis of undescended testicles. Arch. Surg., **31**: 290-300, 1935.

[22] Martin, E.: Surgical treatment of sterility. Univ. Penn. Med. Bul., **15**: 2, 1902. (Cited by Humphreys and Hotchkiss.)

[23] Hagner, F. R.: The operative treatment of sterility in the male. J. A. M. A., **107**: 1851-1854, 1936.

[24] Humphreys, G. A. and Hotchkiss, R. S.: Vaso-epididymal anastomosis. J. Urol., **42**: 815-820, 1939.

[25] MacLeod, J.: Work on hydrogen peroxide producing bacteria. Cited by Hotchkiss, Fertility in Men, Lippincott, 1944.

In the treatment of seminal insufficiencies all measures are used which aim to improve the patient's general health as well as to stimulate spermatogenesis. Of all the endocrine preparations, thyroid is probably most widely employed; it is certainly the least expensive. Its indication would seem to be mainly for those with low basal metabolic rates. Clinical results from the use of gonadotropins are usually disappointing although occasionally of apparently definite value. It is possible that inadequate dosage is used too often. Testosterone in small doses may be of value when there is diminished motility of the spermatozoa, but therapeutic amounts depress spermatogenesis.

A well-balanced diet with adequate proteins, minerals and vitamins is important to maintain good nutrition. Supplementation with multiple vitamins and vitamin E may be indicated in some cases. Obese patients should be reduced. Some patients may require more rest and sleep; others need more exercise and time out-of-doors. Alcohol and tobacco are toxic factors which may need to be eliminated. Tight-fitting or excessive warmth-producing underwear may require modification.

The above general measures have been used in the treatment of cases in this series showing seminal deficiencies. In most patients there has been no appreciable demonstrable change in the seminal findings, although in a few there was definite improvement in spermatozoa counts and in the survival rate of the sperm. As noted above, pregnancies have occurred not infrequently in spite of seminal findings considered to be below the "good" fertility range. Pregnancies eventually occurred in 28 (37.3 per cent) of 75 couples in which the man was classified as being of "intermediate" or "poor" fertility.

There are numerous factors to be considered in the male infertility problem. Possibly there are qualitative and even quantitative factors of which we are yet unaware.

CONCLUSIONS

Two hundred ninety-two men in barren marriages were studied and classified as to their fertility. Of 218 cases with follow-up information, pregnancies occurred in 50.8 per cent of the couples in which the husband was rated as good, in 47.4 per cent of the intermediate group, in 27.0 per cent of the poor group, and in none of the cases where the man was classified as sterile. Pregnancies resulted in 50.6 per cent of couples in which the male gonads were found to be normal on physical examination, in 31.2 per cent of those with unilateral testicular changes and in only 10.9 per cent of those with bilateral testicular changes. The role of the urologist in the study and treatment of problems of male infertility is stressed.

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TRANSLUMBAR SERIAL AORTOGRAPHY: A NEW MEDIUM AND A NEW TECHNIQUE

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INTRODUCTION

From the increasing number of cases of aortograms reported, it is rather obvious that translumbar aortography is becoming a more widely accepted procedure. One of us, in a paper read before this society in 1947, reviewed the technique, indications for, values, and dangers of translumbar aortography. Smith, Rush and Evans have recently reported over 300 translumbar aortograms. The chief source of worry over the possible dangers of aortography has been the lack of a safe contrast medium; indeed, this one objection has led to its lack of universal adoption. Eighty per cent sodium iodide, the most commonly used contrast medium, is quite irritating and seems to have been responsible for several deaths which have followed the procedure. At the writing of this paper, we have had no deaths following aortography. Through personal communications, we know of several deaths which have occurred in other investigators' hands, although none have as yet been reported in the literature. In one case that was reviewed by us in our own territory, the x-rays show that the 80 per cent iodide was inadvertently injected into the superior mesenteric artery instead of into the aorta. Death resulted within 24 hours and postmortem examination showed the entire intestinal tract sloughing, due undoubtedly to the necrotizing effect of the sodium iodide. All deaths of which we are aware have resulted from the accidental injection of the superior mesenteric artery, instead of the aorta, with 80 per cent sodium iodide. It has been realized by all workers in this field that sodium iodide is far from the perfect medium and represents a rather definite hazard. An ideal medium would have a low viscocity, low toxicity, extreme x-ray density, and be nonirritating in the required concentrations. Concentrated diodrast lacks the fluidity to give good pictures and has led to some deaths in a large angiocardiography series which were reported.

Our attention was directed to concentrated (75 per cent) neo-iopax because of its low viscocity and ease of injection. In fact, it is so readily injected if warmed before use, that we now do our injections by hand and have largely discarded the pressure device used initially. Through courtesy of the Schering Corporation we were provided with the concentrated dye to use in our initial experiments. There is little doubt, that while neo-iopax in 75 per cent concentration is irritating to some extent, it is certainly far less irritating than 80 per cent sodium iodide. Its use in routine translumbar aortography has convinced us that while the pictures are not quite as good for reproduction, clinically, it gives almost as good pictures as sodium iodide. Our fears regarding extravasation and possible injection into the mesenteric arteries have definitely been lessened. In several cases of extravasation, no ill effects have been apparent. We have, thus far, been

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Read at annual meeting, South Central Section, American Urological Association, Tulsa, Okla., September 25, 1950.

fortunate in not injecting the superior mesenteric artery with either neo-iopax or sodium iodide. Neo-iopax is admittedly not the final word in media for this work, and we are at present working on another medium which may prove to be much less irritating.

The other great disadvantage of aortography, as commonly used, has been that one has been limited to one picture made during injection, which shows the renal blood flow, and a second made just after the injection, when the dye outlines the kidney, the so-called nephrogram. In one of our earlier routine translumbar aortography cases, an unexplained block was seen in an artery which was not confirmed 6 months later when the patient died of carcinomatosis and an autopsy was done. Following that case, we began to try to secure serial x-rays, which would give us a number of pictures of the dye flowing into and out of the kidneys. Our interest in securing such x-rays was further stimulated by the challenging new concepts of Trueta. In the light of this new idea of renal physiology, based on the experimental demonstration of two renal circulations under autonomic nervous control, it might be possible to show such a vascular shunt by serial aortography. Recent confirmatory reports of Trueta's experimental findings attest to the universal interest which this work has aroused.

The expense of most serial x-ray devices was an initial complete barrier to our efforts until we came upon the "seriograph." This device was once considered and discarded because it is limited to 10 by 12 inch films, but we found it to be adequate if the patient was very carefully positioned and preliminary films made to insure that all of the renal areas were on the film. This device carries a clip of six films, all of which can be exposed automatically, in either 4½ or 12 seconds as desired. It was obvious from the first successful pictures, that 6 views made while the dye was running in permitted a far more accurate picture of the renal circulation than just one.

Recently we have also secured excellent pictures with either of two homemade devices designed, one by Dr. D. C. Weir and the other by Dr. A. E. Brodeur of the Department of Radiology, St. Louis University. Since Dr. Brodeur's apparatus is automatic, and will probably be available commercially, only a brief description is given of Dr. Weir's device. It consists of a tunnel constructed of masonite and is lead lined, except for a space in the center which is covered by a grid. The grid is so centered that if four 10 by 12 cassettes are inserted in order, when the last one is placed flush with the open end of the tunnel, the first is directly under the grid. The patient is, of course, correctly positioned over the grid. Blocks of wood are cut to the same size as the cassettes to use in exposing the last films. As soon as one exposure is made, another cassette, or block, is pushed in and another exposure can be made. With practice, 5 to 7 exposures can easily be made in 7 to 10 seconds. The device can be made by almost anyone at a total cost of around ten dollars.

CLINICAL USE

The value of serial aortography can best be illustrated by the following case histories. In the first case to be presented, we have shown by serial translumbar aortography the presence of a renal artery embolus which appears as though it is becoming recanalized. A second series, however, done 4 months later, shows complete obliteration of the artery. As far as we can determine, this was the first time that serial translumbar aortography was performed. It is also the first time anyone has demonstrated radiographically a fresh embolus of the renal artery.

CASE REPORTS

Case 1. R. W., aged 44 years, was admitted through the emergency room of St. Louis City Hospital to the surgical service because of sudden severe right loin and abdominal pain with nausea and vomiting. The past history was significant in that 6 months previously, while at work as a machinist, he developed sudden, severe precordial and chest pain and became dyspneic. Work-up was done at another hospital, where the patient was told he had had a "heart attack" and that his heart was "irregular." An abstract of his clinical record from this hospital showed that the patient had auricular fibrillation and was discharged on digitalis. As soon as it was determined that this was not an acute surgical problem, the patient was transferred to the urological service. On transfer to our urological service, examination showed right lumbar tenderness, spasm and guarding without radiation of pain. Urinalysis showed a clear urine, specific gravity 1.021, pH 6.0, negative albumin and sugar. Microscopic examination showed a few epithelial cells, red cells, and clumps of white cells. The patient was given adanon with relief of pain. An excretory urogram made immediately showed good function on the left, with absolutely no function even in 30 minutes on the right (fig. 1, *A*). The diagnosis of a possible nonopaque stone was made. Cystoscopy was carried out the following day and the bladder was normal except for the edema of the right orifice. There was no urine and no intravenous indigo carmine on the right. Catheters were introduced easily and the right pyelo-ureterogram was completely normal (fig. 1, *B*). An electrocardiogram showed left ventricular preponderance, auricular flutter with fibrillation and myocardial changes. For

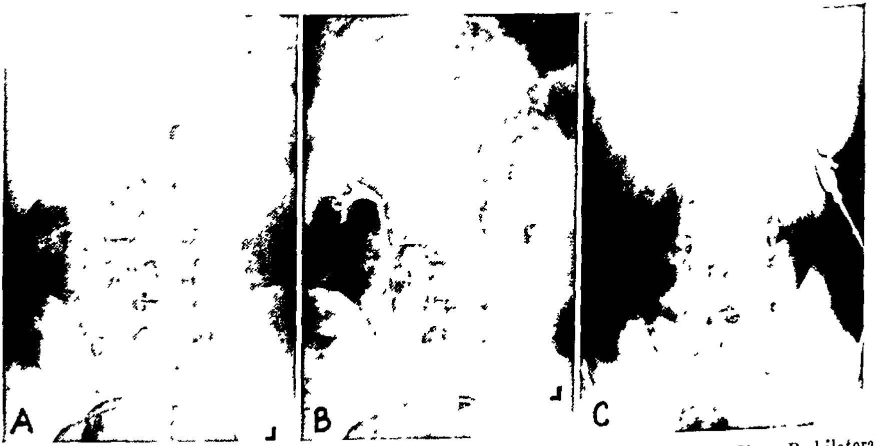

FIG. 1. *A*, normal left pyelogram, no function on right, 30 minute film. *B*, bilateral, normal retrograde pyelo-ureterograms. *C*, translumbar aortogram made with 75 per cent neo-iopax. Normal left renal blood flow, no dye enters right renal artery.

these reasons the clinical diagnosis of right renal infarction was made. An ordinary translumbar aortogram was then made with 75 per cent neo-iopax and showed a failure of the right renal artery to fill with dye, which confirmed the clinical impression (fig. 1, *C*). Serial aortograms made 4 days later showed clearly

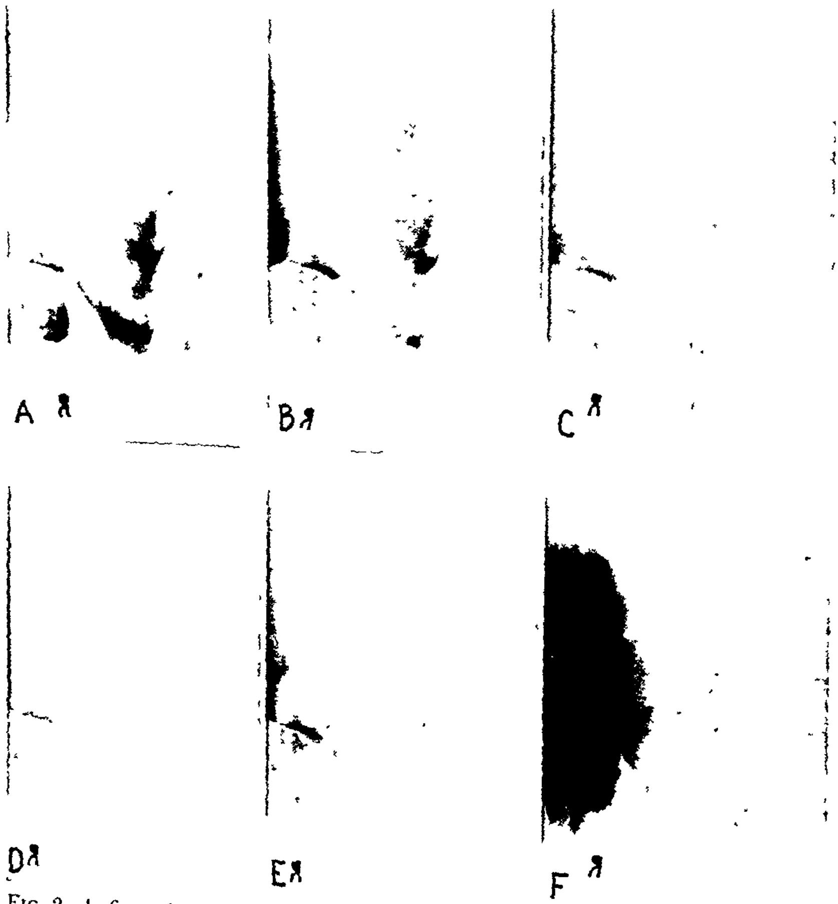

FIG 2 *A*, first of a series of 6 films made in 4½ seconds as 75 per cent neo-iopax is injected into aorta. Compare with figure 3. *B*, second film in series. Compare with *A* and figure 3 *C*, third film in series. Compare with *A* and *B* and figure 3. *D*, fourth film of series. Compare with *A*, *B*, *C* and figure 3. *E*, fifth film in series. Compare with *A*, *B*, *C*, *D*. *F*, last film in series. Compare with *A*, *B*, *C*, *D*, *E*.

an intra-arterial clot with some slight blood flow past the obstruction. All six exposures were made within 4½ seconds, and the first picture was made just as the injection into the aorta was completed (fig. 2). Because of the rapidity of exposure, contrast of the x-rays is not good and a diagrammatic sketch of the first four serial films (fig. 2, *A*, *B*, *C*, *D*) is shown in figure 3 to show progression of the dye around the embolus. These can be compared with the reproduction of the x-rays (fig. 2).

Embolectomy was considered, but the patient suddenly developed a thrombophlebitis of the left leg, and the operation was cancelled. The cardiologist was of the opinion that the previous episode of chest pain represented a coronary attack with thrombus formation on the ventricular wall. The right renal embolus

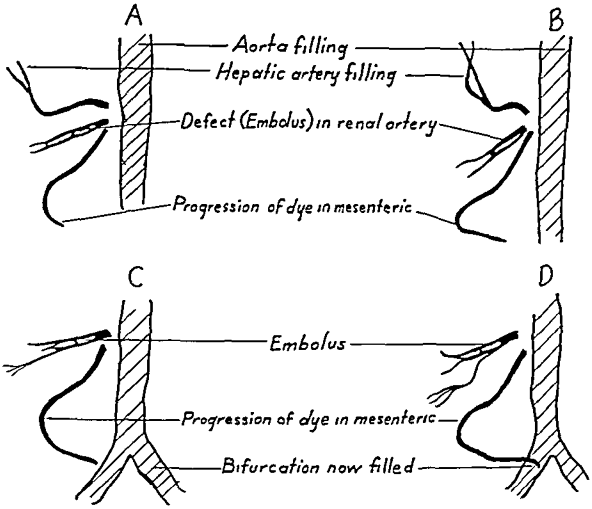
A
B
Aorta filling
Hepatic artery filling
Defect (Embolus) in renal artery
Progression of dye in mesenteric
C
D
Embolus
Progression of dye in mesenteric
Bifurcation now filled

FIG. 3. Schematic reproduction of progression of dye around embolus in right renal artery. Progression of dye in neighboring vessels also shown for comparison. Compare *A* with figure 2, *A*; *B* with figure 2, *B*; *C* with figure 2, *C*; *D* with figure 2, *D*.

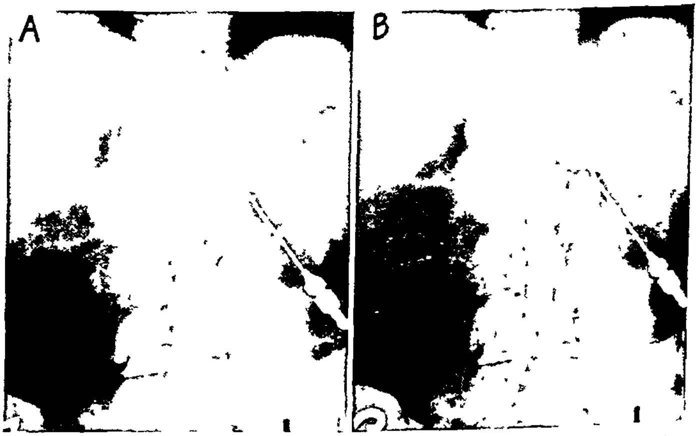

FIG. 4. *A*, fourth film of a series of six, exposed in 4½ seconds, 4 months after serial films in figure 2. Left renal blood flow is normal. Complete block of right renal artery. Embolus previously shown has obliterated right renal artery. *B*, last film of series of six, shows no dye in right renal artery although dye in aorta has now filled bifurcation and iliacs. Compare *B* with *A*, which shows column of dye in aorta to be at approximately third lumbar vertebra, and bifurcation not yet filled.

came from this source. The patient was transferred to the cardiology service where the prothrombin time was maintained between 20 and 23 per cent by dicumerol and heparin. The patient improved and was discharged 1 month later.

The patient was re-admitted for examination 4 months later. The only symptoms were an occasional swelling of the left leg and pain. There were no urinary symptoms. During the 4 month interval, urinalyses had been normal, the blood pressure had been normal, but the fibrillation persisted. Physical examination on admission was normal except for fibrillation. Routine laboratory examinations were normal. Excretory urography showed a normal functioning left side with no dye excretion on the right. Serial translumbar aortography with 18 cc of 75 per cent neo-iopax showed a complete failure of the dye to enter the right renal artery (fig. 4). He had no reaction to this examination and was discharged the following day. From the standpoint of the Goldblatt phenomenon it is of interest to note that although during both hospitalization periods his blood pressure was carefully checked several times a day, the range was from 122 to 130 systolic and 75 to 78 diastolic.

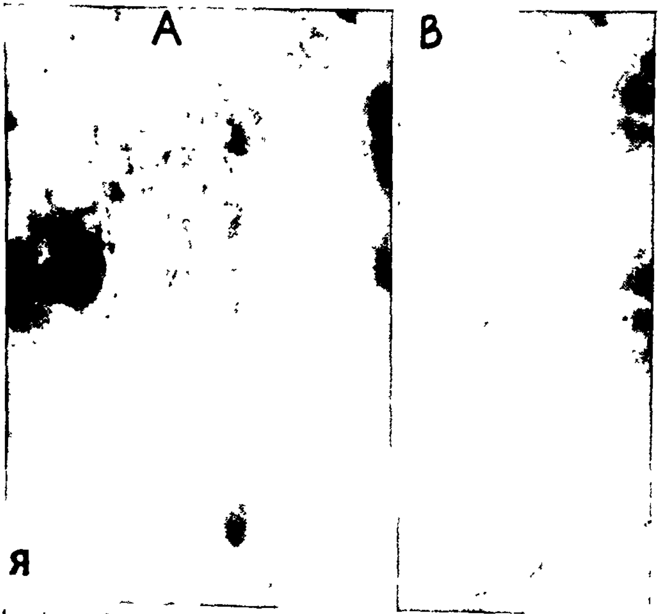

FIG. 5. *A*, retrograde pyelograms showing normal right side with filling defect in middle calyx on left. *B*, repeat left pyelogram with more filling, but defect still present in middle calyx.

Case 2. M. H., a 48 year old man, was admitted to St. Mary's Hospital with acute left renal colic and gross hematuria. Cystoscopy the following morning disclosed no ureteral obstruction, and no calculi were visible on the flat film. Bizarre pyelograms suggestive of a left renal tumor were obtained (fig. 5). Because of this, and because the patient continued to have severe left renal colic although the red cells disappeared from the urine, serial aortography was carried out (fig. 6). An excretory urogram made 5 minutes after the aortogram again suggested a space occupying lesion in the left renal parenchyma (fig. 7). These showed no displacement of the renal vessels and no frank pooling of the dye but a suggestion of diffusion of the dye over a small area in the renal parenchyma consistent with the suspected mass. Exploration revealed the correct interpreta-

Embolectomy was considered, but
phlebitis of the left leg, and the op
of the opinion that the previous epi-
attack with thrombus formation on th

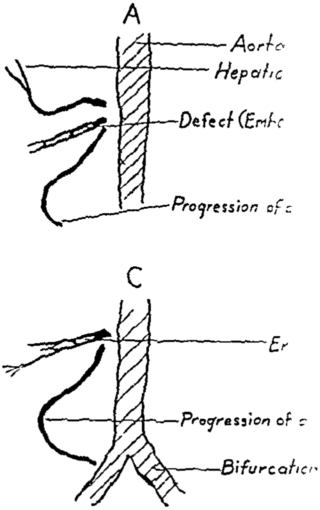

FIG. 3. Schematic reproduction of progres
artery. Progression of dye in neighboring vess
with figure 2, *A*; *B* with figure 2, *B*; *C* with figu

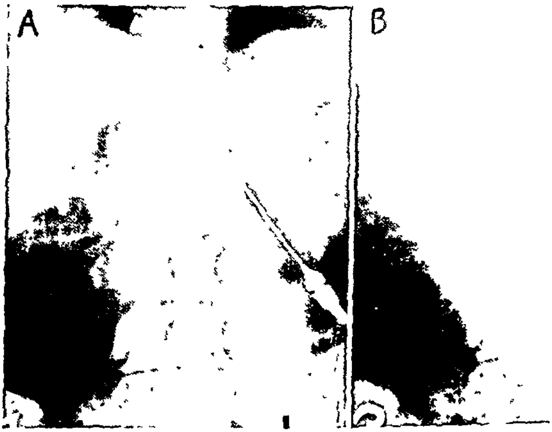

FIG. 4. *A*, *fourth film of a series of six*, exposed in $4\frac{1}{2}$ seconds, 4 month
in figure 2. *Left renal blood flow is normal.* Complete block of right renal
previously *shown has obliterated right renal artery*. *B*, last film of series o
dye in right *renal artery* although dye in aorta has now filled bifurcation and
pare *B* with *A*, which shows *column* of dye in aorta to be at approximately t
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where the prothrombin time was maintained between 20 and 23 per ce
dicumerol and heparin. The patient improved and was discharged 1 month la

The patient was re-admitted for examination 4 months later. The only sym
toms were an occasional swelling of the left leg and pain. There were no urinar

tion of these films. A small cyst filled with old blood was found with extensive hemorrhage into the surrounding renal tissue.

These sets of pictures not only show the dye entering the renal arteries and the arterial distribution, but also the dye passing out through the renal veins. We believe that this is the first time that the complete renal circulation in a human being has been shown by the translumbar route.

DISCUSSION

Keller Doss is the father of the statement that "the kidney is no better than its blood supply." We agree with this statement wholeheartedly. The blood supply of any organ is, however, a dynamic, ever changing force, and even in shock states is not static as Trueta's experiments so clearly show. For this reason alone then we propose that serial pictures showing progression of the blood through the kidneys will be of far more value than the single aortogram. Its use undoubtedly will bring up far more difficulties of intrepretation, which admittedly we have only begun to work out.

It is suggested that perhaps some day serial aortograms can confirm or disprove the concept of an intrarenal shunt in lower nephron nephrosis. Serial pictures have all of the advantages of the routine translumbar aortograms as well. These have been repeatedly listed in the literature and there is no need to enumerate them again.

Certainly enough cases of translumbar aortography have been reported in the literature to be sure that there is no danger from hemorrhage following aortic puncture and that surrounding structures will not be inadvertently damaged. The only danger lies in the possibility of throwing a necrotizing medium into the superior mesenteric artery with resultant gut necrosis and death of the patient. This last remaining danger can be overcome if we have a less toxic medium. While 75 per cent neo-iopax is admittedly not a completely safe medium, it is certainly safer than 80 per cent sodium iodide. The small loss in x-ray opacity which occurs when 75 per cent neo-iopax is used instead of 80 per cent sodium iodide is more than compensated for by the increased safety. The ideal medium would approach the x-ray opacity of thorotrast and yet be nontoxic. in needed concentrations, if accidentally injected into the mesenteric arteries.

SUMMARY

The successful use of 75 per cent neo-iopax is reported as a substitute for the more irritating sodium iodide, in translumbar aortography.

The resultant slight loss in x-ray detail is compensated for by its greater safety.

Serial aortography can be done with simple, inexpensive equipment and adds tremendously to the value of aortography.

Radiographic visualization of an embolus in the renal artery and of both the renal arteries and veins is believed to have been shown for the first time.

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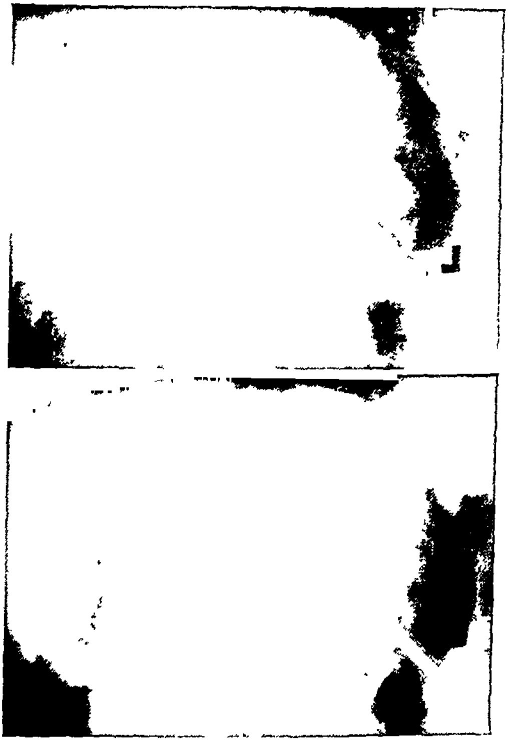

Fig. 6. *A*, second film in serial translumbar aortogram with 75 per cent neo-iopax. Renal arteries well shown, *no deviation and no frank pooling*. Suggestion of dye pooling in region of suspected mass. Note dye in aorta for comparison with *B*. *B*, last film in serial aortograms. *Dye has left aorta and renal arteries and now renal veins are* well visualized, especially on left.

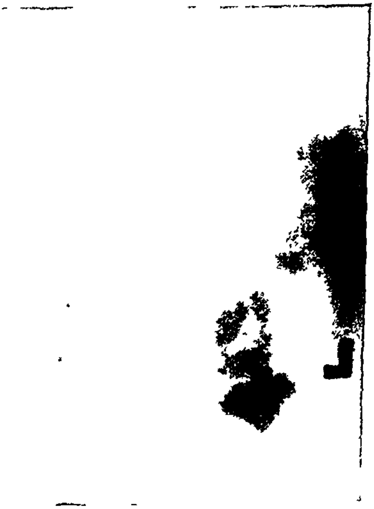

Fig. 7. Excretory urogram made by *taking another* x-ray 5 minutes after last serial aortogram. Filling defect still present on left pyelogram.

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REFERENCES

ARCADI, J. A. AND FARMAN, F.: Experimental studies and clinical aspects of renal circulation. J. Urol., **62**: 756, 1949.

GOODWIN, W. E., SLOAN, R. D. AND SCOTT, W. W.: The "Trueta" renal vascular shunt. J. Urol., **61**: 1010, 1949.

MELICK, W. F. AND VITT, A. E.: The present status of aortography. J. Urol., **60**: 321, 1948.

SANCHEZ-PEREZ, J. M. AND CARTER, R. A.: The time factor in cerebral angiography and an automatic seriograph. Am. J. Roentgenol., **62**: 509, 1949.

SMITH, P. G., RUSH, T. W. AND EVANS, A. T.: Technique and values of translumbar aortography. J. Urol., **65**: 911, 1951.

VITT, A. E. AND MELICK, W. F.: Studies on translumbar aortography. J. Mo. State Med. Assoc., **44**: 749, 1947.

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Vol. 66, No. 3, September 1951
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ARTERIOGRAPHY AS OBSERVED IN 80 PATIENTS AT ST. LOUIS CITY HOSPITAL

GRADY WATTERSON REAGAN, JR. AND GRAYSON CARROLL

The practical value of arteriography and the hazard connected with the procedure are only to be determined by the recital of experiences with its use. The resident staff of St. Louis City Hospital has studied some 80 patients with arteriography and the experiences and observations made in this series emphasize certain features which are here recited.

The hazards, practical or theoretical, are listed by Smith, Rush and Evans as 1) fear of hemorrhage following procedure; 2) extra-aortic injection of contrast medium; 3) acute iodinism; 4) allergic reaction; 5) mesenteric thrombosis; 6) perforation of an intraperitoneal viscus; 7) pneumothorax; 8) aortic intramural injection; 9) injection of full quantity of contrast medium into a branch of the aorta.

Our experiences with these hazards are as follows: Two cases of extra-aortic injection of contrast medium which caused the patients some pain over the injection site; 1 case of partial injection into the superior mesenteric artery. This artery and its branches were the only vessels outlined aside from the aorta and external iliacs. There was no morbidity from this technical error.

Clinically traumatic hemorrhage has not occurred. Certain simple precautions need to be taken, however. Our needle is especially constructed so that the bevel is ⅛ inch in length, the gauge 17, and the length of the needle 6½ inches.

The aorta should be entered on its posterior lateral aspect on the level of the twelfth thoracic vertebra and maintained in that position. We had opportunity to study the site of puncture in one of our patients who died of inoperable papillary carcinoma of the kidney pelvis 6 weeks following arteriography. No puncture site or peri-aortic reaction could be found in the autopsy specimen. This hazard is more a fear than a fact.

Extravasation of medium into surrounding tissue, rather than into the aorta, is possible but should occur very infrequently since the return flow of blood is so obvious when the needle is within the lumen. However, we had one complete extravasation. This occurred on the first case with the high pressure apparatus. The patient complained of moderate pain over the injection site for 3 or 4 days.

Partial extravasation occurred in a patient in whom the syringe was forcibly pushed against a table to produce rapid injection of the medium. The patient experienced some pain which was transient, but no other symptoms.

In the last 49 patients we have used ordinary hand injection taking 3 or 4 seconds for the injection and obtained satisfactory arteriograms without complications.

It is often asked: "What happens to the 15 cc of 80 per cent sodium iodide solution injected directly into the arterial circulation?" The iodides are distributed in the same manner as the chlorides and bromides. It is entirely extracellular, penetrating only the red blood corpuscles. The iodide ion is readily

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Read at annual meeting, South Central Section, American Urological Association, Tulsa, Okla., September 25, 1950.

excreted by the kidney, probably preferentially over chlorides, for most of the ion is lost in 24 hours. The excretion of iodide may be hastened by giving large doses of chlorides.

Ascorbic acid in large doses may hasten the elimination of the iodide ion Very little iodide is retained and that which does remain is in organic combination.

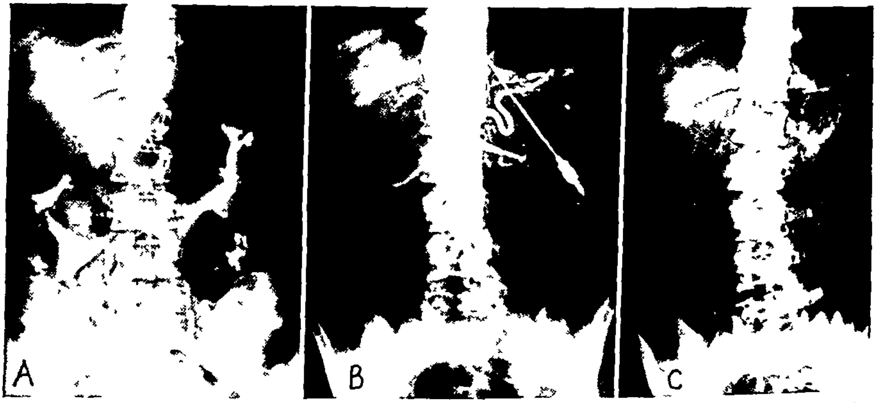


FIG. 1. *A*, retrograde pyelogram shows typical polycystic kidneys. *B*, aortogram shows wider spacing of secondary artery branches than normal due to cysts. *C*, renogram reveals large, ill defined, and bizarre kidney shadows.

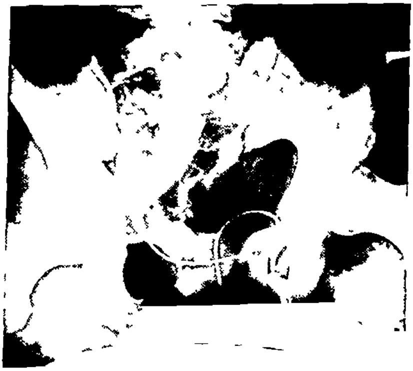


FIG. 2. Retrograde pyelogram shows solitary kidney lying in front of sacrum.

Markedly impaired renal function should be a contraindication for arteriography, especially in patients whose renal reserve is low from malignant hypertension.

Allergic reaction may occur and should be given the same consideration as when administered in pyelography.

The highly concentrated solution is irritating and when injected in smaller vessels it may cause its complete occlusion.

Fatalities have been reported due to the injection being made below the coeliac axis causing a large amount of medium to enter the superior mesenteric artery with resultant gangrene of the intestine. This technical error can be avoided by observing reasonable care in not injecting below the twelfth thoracic vertebra. Smith, Rush and Evans state: "Accidental superior mesenteric artery injection of contrast medium results in mesenteric thrombosis because of one or a combination of the following: 1) use of too great a quantity of contrast medium, 2)

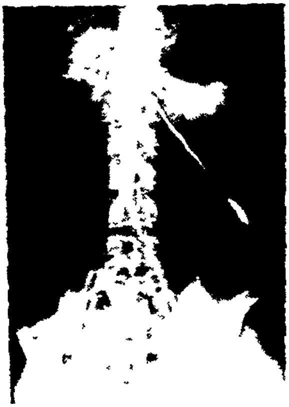


FIG. 3. Shows solitary renal artery of good size. Exact point of origin cannot be demonstrated.

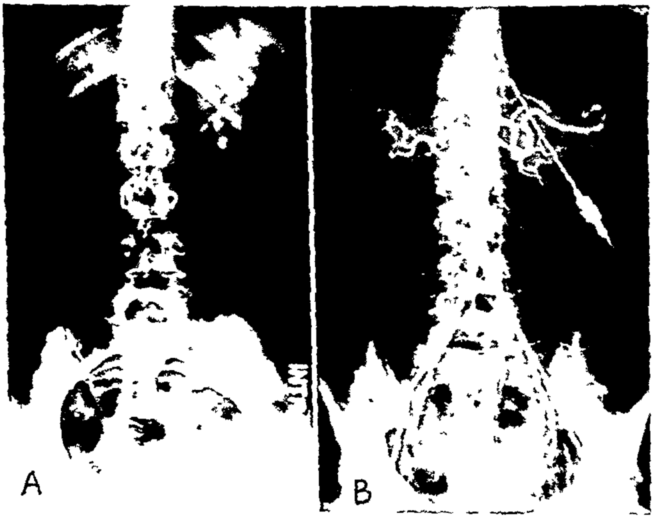


FIG. 4. A, no appearance of medium in right kidney pelvis or calyces on excretory urogram B, very minute right renal artery. Left renal artery is normal in size distribution. Patient has grade 3 carcinoma of the cervix.

too great an injection pressure, or 3) the use of too toxic and irritating a contrast medium."

No ill effects have been noted in the aged having arteriosclerosis in varying degrees.

Patients with known tuberculosis and thyroid disease have not been subjected to the study on a theoretical basis.

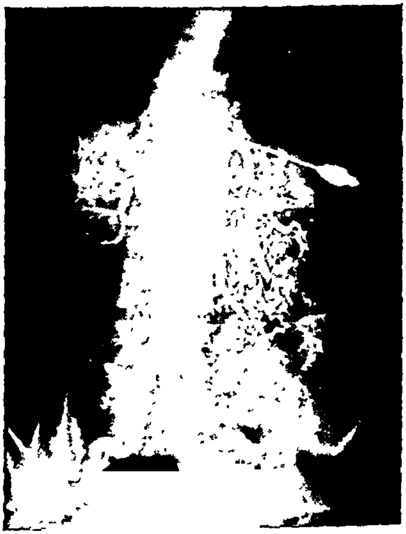


Fig. 5. Aortogram shows sudden occlusion of left secondary renal branch with marked puddling of dye in lower portion of kidney. Typical aortogram of hypernephroma. Catheter could not be passed up this ureter. Patient died 1 year later, a large hypernephroma (800 gm.) of left kidney being found at autopsy. It replaced lower pole of left kidney propagating tumor into renal vein.

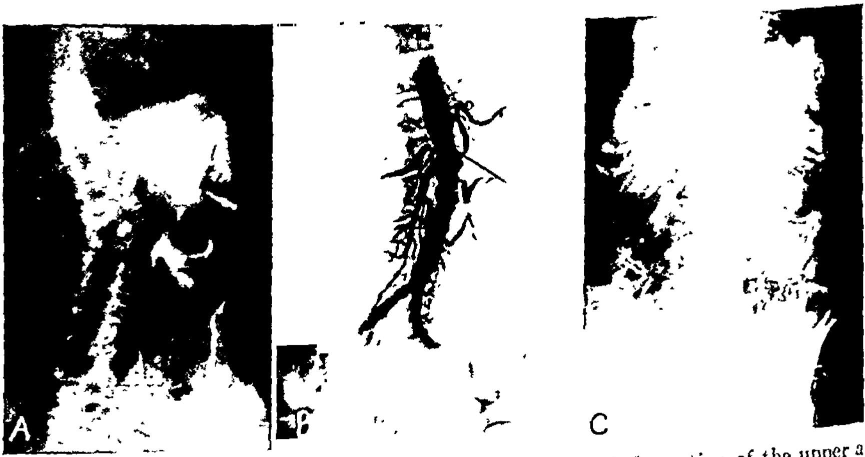


Fig. 6. *A*, left retrograde pyelogram shows flattening and elongation of the upper and middle calyces with a downward depression of the middle calyx suggesting a space occupying mass. *B*, aortogram shows two major or primary renal arteries to left kidney with depression upward of upper artery secondary branches and depression downward of lower artery secondary branches. Note arteriosclerotic changes of aorta and iliac vessels as well as origin of visceral branches. Absence of right renal artery. *C*, left nephrogram shows circular area of radiolucency in mid-portion of kidney without blood supply characteristic of cyst.

The procedure requires hospitalization, a short anesthetic, the cooperation of the x-ray technician. The technical ability to perform the procedure may be acquired in a short time if a thorough knowledge of the regional anatomy is acquired beforehand. Attention to detail, teamwork, and proper preoperative evaluation of the patient's condition are essential for good results. We have had no experience with arteriography in children.

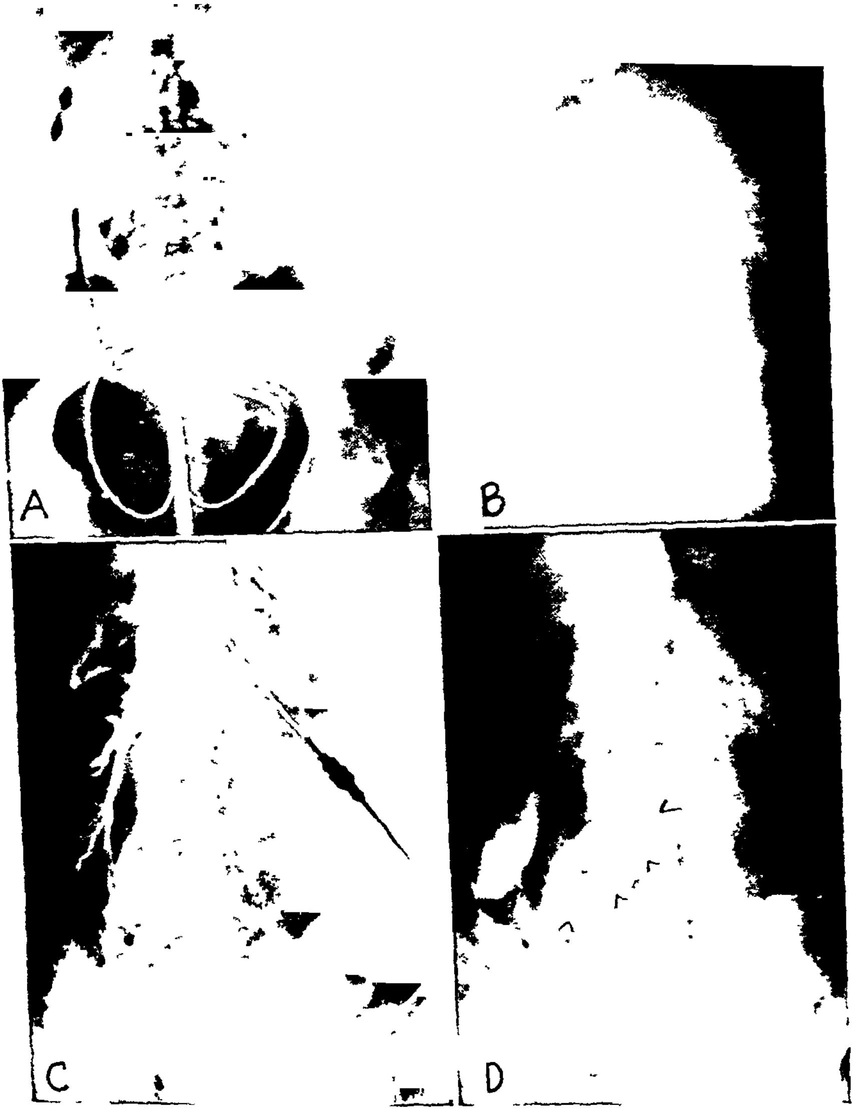
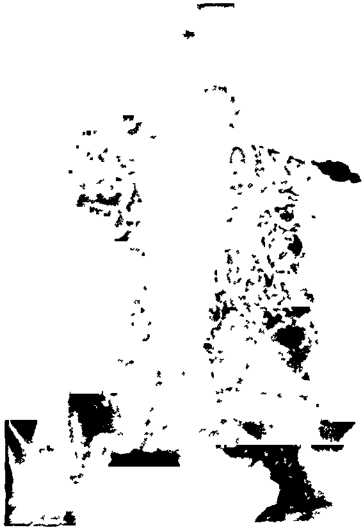


FIG. 7. *A*, retrograde pyelogram; left kidney and ureter are pushed downward and to right. Large palpable mass on left side of abdomen. *B*, lateral pyelogram shows ureter and kidney markedly anterior. *C*, aortogram shows splenic artery on right side. Left renal artery not visible. *D*, nephrogram shows left kidney to right, overlying fourth and fifth lumbar vertebrae in an oblique position. Right nephrogram easily seen.

THE VALUE OF ARTERIOGRAPHY

The value of the procedure was demonstrated in many instances in this series better described in the individual arteriograms to be presented (figs. 1 to 8). This series indicated its usefulness in the following:

1. Differential diagnosis of renal masses.
   a) Hypernephroma.



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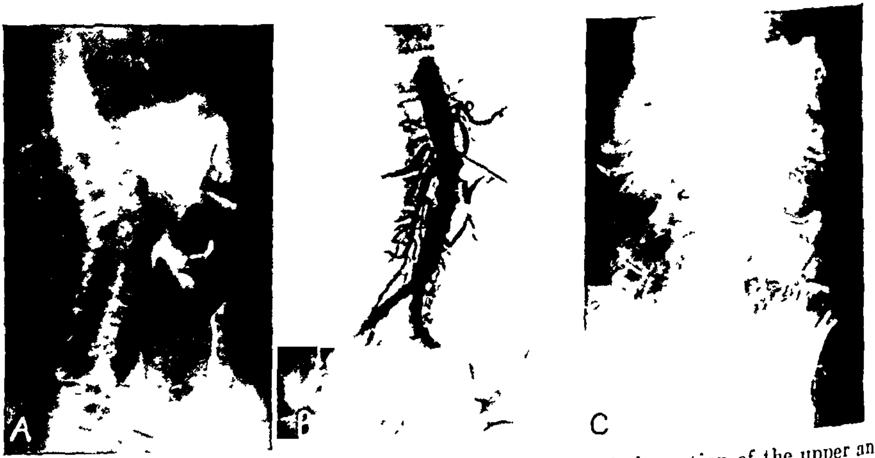

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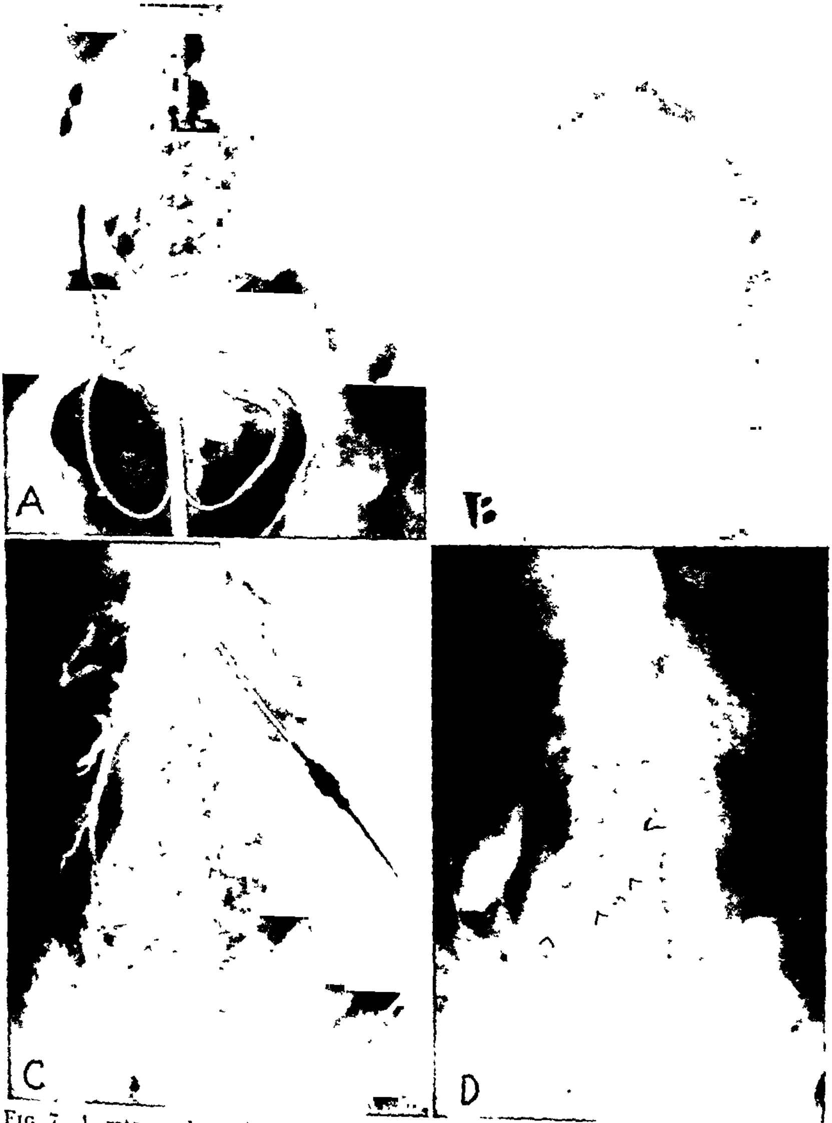

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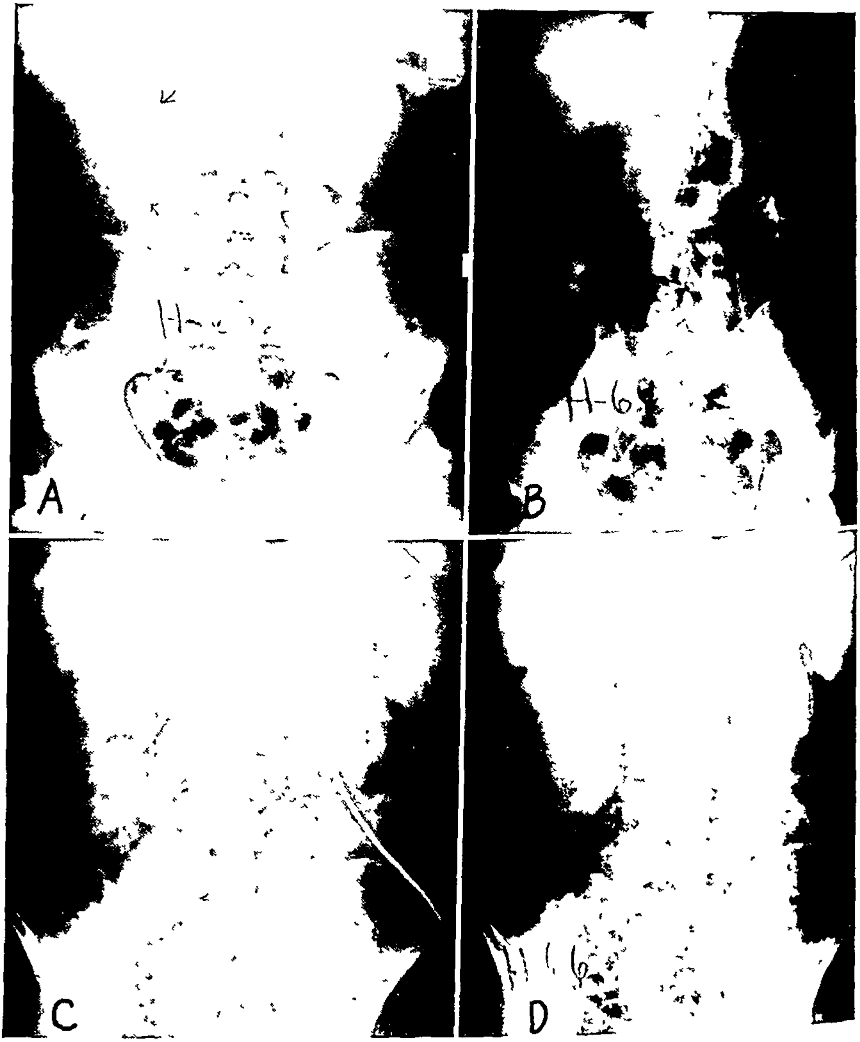

FIG 8. *A*, plain urogram shows smooth round mass in right kidney area. *B*, pyelogram shows a mild hydronephrosis without suggestion of a space occupying mass within kidney. *C*, aortogram shows blood supply to mass derived from right renal artery. *D*, renogram reveals major portion of right kidney to be replaced by mass Also in certain areas around inner half of periphery, density is somewhat more dense than surrounding parenchyma while in outer portion of mass it is less dense Diagnosis· Cystadenocarcinoma of right kidney as proved by nephrectomy.

- b) Polycystic disease.
- c) Solitary cyst.
- d) Hydronephrosis.
- e) Retroperitoneal tumors not arising from the kidney.
- f) Horseshoe or ectopic kidney.

2. Operative procedures indicated.
    - a) Scanty blood supply to a hydronephrotic kidney, indicating nephrectomy rather than plastic repair.

  - b) Renal vein involvement in hypernephroma, suggesting inoperable condition.
  - c) Distribution of renal blood supply, suggesting heminephrectomy in certain cases of renal calculus with calyectasis.
3. Aneurysms.
  - a) Aneurysm of renal artery.
  - b) Aneurysm of aorta and other branches.

SUMMARY

Translumbar arteriography is relatively safe if the procedure is performed by one with detailed knowledge of the regional anatomy, adequate skill of performing the procedure and attention to detail in such performance. Proper preoperative evaluation of the patient's renal, cardiac, and liver reserve should be made. Sensitivity to contrast medium should be checked. The cases most likely to benefit from arteriography are those in which the diagnosis, prognosis, and management of the existing renal disease cannot be definitely stated by the previous urological workup.

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Humboldt Bldg., St. Louis 3, Mo. (G. C.)

REFERENCES

Carter, W.: Personal communications.
Doss, A. K., Thomas, H. C. and Bond, T. B.: Renal arteriography, its clinical value. Texas State J. Med., 38: 277-280, 1942.
Doss, A. K.: Renal hypertension. The value of translumbar arteriography in its diagnosis. A preliminary report. Texas State J. Med., 39: 188-194, 1943.
Doss, A. K.: Translumbar aortography: Its diagnostic value in urology. J. Urol., 55: 594-606, 1946.
Doss, A. K.: Translumbar aortography: An apparatus for injecting the radiopaque media. Surgery, 16: 422-424, 1944.
Doss, A. K.: The management of ureteropelvic juncture obstruction: Translumbar aortography an adjunct. J. Urol., 57: 521-538, 1947.
Gnose, D.: Personal communications.
Hartnett, L. J.: Visualization of the maternal circulation at the site of the placenta (placentagrams) J. Missouri State M. A., 44: 754, 1947.
Hartnett, L. J.: Personal communications.
Henline, R. B. and Moore, S. W.: Renal arteriography; Preliminary report of experimental study. Am. J. Surg., 32: 222-229, 1936.
Kinman, L.: Personal communications.
Melick W. F.: Personal communications.
Nelson, O. A.: Arteriography of abdominal organs by aortic injection: A preliminary report. Surg., Gynec. and Obst., 74: 655-662, 1942.
Nelson, O. A.: Arteriography in renal and abdominal conditions. J. Urol., 53: 521, 1945.
Price, A. H. and Wagner, F. B., Jr.: Complete occlusion of the abdominal aorta: Report of two patients diagnosed by aortography. Surg., Gynec. & Obst., 84: 619-624, 1947.
Smith, P. G., Rush, T. W. and Evans, A. T.: an evaluation of translumbar arteriography. J. Urol., 65: 911, 1951.
Vitt, A. E. and Melick, W. F.: Studies on translumbar aortography: A simple apparatus for translumbar aorteriography. J. Missouri State M. A., 44: 749-754, 1947.
Wagner, F. B., Jr.: Complications following arteriography of peripheral vessels. J. A. M. A. 125: 958-961, 1944.
Wagner, F. B., Jr.: Arteriography in renal diagnosis; Preliminary report and critical evaluation. J. Urol., 56: 625-635, 1946.
Wagner, F. B., Jr., Price, A. H. and Swenson, P. C.: Abdominal arteriography: Technique and diagnostic application. Am. J. Roentgenol., 58: 591-598, 1947.
Wagner, F. B., Jr. and Price, A. H.; Fatality after abdominal arteriography. Surgery, 27: 121-626, 1950.
Yarbrough, C.:Personal communications.

SCIENTIFIC PROGRAM, MEETING OF NORTH CENTRAL SECTION, AMERICAN UROLOGICAL ASSOCIATION, COMMODORE PERRY HOTEL, TOLEDO, OHIO OCTOBER 4-6, 1951

OCTOBER 4

Obstructive Uropathies in Children. Frank Bicknell, Detroit, Mich.

Wilms Tumors in Children. Robert Garrett and H. O. Mertz, Indianapolis, Ind.

Delayed Cystograms in Children. Raymond G. Bunge, Iowa City, Iowa

Traumatic Injury of the Kidney in Children. H. O. Mertz, Indianapolis, Ind.

Ureteral Tumors. William Baker and Edwin Graf, Chicago, Ill.

Carcinoma of the Scrotum with New Approach to Gland Dissection. Marion W. Coleman, R. P. Joyce (by invitation) and Richard Graves (by invitation), Dayton, Ohio

PANEL DISCUSSION........................Urologic Emergencies

Panel: James Sargent
James Joelson
William Baker
Gershom Thompson

Moderator: William Engel.

Bilateral Spontaneous Peri-renal Hematoma. Gustave Link, Toledo, Ohio

Perirenal Insufflation by Cannula. Harry Trattner, Cleveland, Ohio

Advantages of Cherny Incision. Ormond Culp and James DeWeerd (by invitation), Rochester, Minn.

Cushing's Syndrome. Problems in Diagnosis and Management. Eugene Poutasse (by invitation), Cleveland, Ohio

BRIEF TOPICS AND USEFUL AIDS

Ectopic Ureteral Orifices. L. F. Huffman, Cleveland, Ohio

Prolapsed Ureterocele. Gershom Thompson, Rochester, Minn.

Trichomonas Urethritis and Stricture. William Butler, Grand Rapids, Mich.

An Improved Method of Rating the Percentage of Active Sperm. Russell Herrold, Chicago, Ill.

An Inhalant Analgesic of Assistance in Minor Urologic Procedures. Robert Breakey, Lansing, Mich.

Carcinoma of the Prostate with Unusual Type of Metastases. John Ryan, Grand Rapids, Mich.

The Nesbit Sign. Rigdon Ratliff, Ann Arbor, Mich.

Xanthine Stone—Difficulty in Diagnosis. William Taylor, Columbus, Ohio

Papillary Renal Pelvic Tumor in a Child. Richard Crowell and William J. Butler, St. Joseph, Mich.

Hodgkin's Infiltration of the Prostate with Preoperative Diagnosis. Leo Prins, Albert Lea, Minn.

An Automatic Valve for the Resectoscope. Leo Prins, Albert Lea, Minn.

An Aid to Control of Immediate Postoperative Bleeding. Raymond Bunge, Iowa City, Iowa

Balanced Suspension to Facilitate Endoscopic Examination. Harry Trattner, Cleveland, Ohio

Use of Panendoscope in Passing a Filliform. Richard Graves, Dayton, Ohio

Excretory Urogram with Pelvic Extravasation. Charles G. Weller, Aurora, Ill.

Fibrocanalicular Hamartoma of the Kidney. A. A. Roth, Cleveland, Ohio

Hypernephroma of Kidney with Metastasis to Thyroid. William Engel, George Crile, Jr., and William Dempsey, Cleveland, Ohio

OCTOBER 5

ONE STAGE PELVIC EVISCERECTOMY FOR PRIMARY CARCINOMA OF THE VAGINA. Arthur Roth, Cleveland, Ohio

THE ANATOMY AND TECHNIC OF HYDROCELECTOMY. Rigdon Ratliff, Ann Arbor, Mich.

LUMBAR URETEROLITHOTOMY. William N. Taylor, Columbus, Ohio

UNUSUAL TYPES OF PROSTATIC CARCINOMA. Gershom Thompson, Rochester, Minn.

TREATMENT OF OLIGOSPERMIA WITH SMALL DOSES OF STILBESTROL. Russell Herrold, Chicago, Ill.

A STUDY OF THE EFFECTS OF BANTHINE ON THE HUMAN BLADDER. Jack Lapides, Austin Dodson, Jr., Ann Arbor, Mich.

President's Address: PRIMARY CARCINOMA OF THE URETER. William Wishard, Indianapolis, Ind.

KIDNEY TRANSPLANT STUDIES. Carl Davis, Jr. (by invitation), Chicago, Ill.

OCTOBER 6

PYELOGRAM CLINICS

9:00 to 11:00 a.m.

All members of the American Urological Association are invited. Those wishing to attend the meeting should contact Dr. James A. H. Magoun, 2001 Collingwood Avenue, Toledo 2, Ohio.

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ADRENAL CORTICAL CARCINOMA IN CHILDREN

ROBERT A. GARRETT

*From the Department of Genito-Urinary Surgery, Indiana University School of Medicine'
Indianapolis, Ind.*

With the increasing study of adrenal cortical activity in the past two decades has come a better understanding of the functioning tumors of the adrenal cortex. The more recent contributors to the literature on this subject, notably Walters[1] and Cahill[2] are in essential agreement on a general classification of these neoplasms, based upon their clinical manifestations of hormonal activity, as follows: 1) Nonhormonal, those displaying no endocrinologic activity; 2) androgenic, those elaborating excess masculinizing steroids; 3) estrogenic, those elaborating excess feminizing steroids; 4) androgenic plus other metabolic hormones, those displaying clinical features of masculinization and Cushing's disease; 5) metabolic tumors without androgens, those displaying Cushing's disease without masculinization; 6) metabolic tumors of one function, those manifesting one metabolic disorder.

The physiology underlying the clinical behavior of such adrenal tumors is complex. The reader is directed to excellent papers on this subject by Kenyon[3] and Cahill[4] where it is discussed in detail. It is sufficient to state that the adrenal cortical steroids isolated to date are numerous and their interrelation not completely understood. There appear to be, however, three main groups functionally: 1) Those bringing about secondary sexual characteristics, viz. estrone (estrogenic) and testosterone (androgenic); 2) those concerned with regulation of electrolyte balance, viz. desoxycorticosterone; 3) those concerned with carbohydrate, protein and fat metabolism, viz. corticosterone, dehydrocorticosterone and others. The interplay between these steroids and other endocrine structures is of even greater complexity, and is the subject of intense investigation today. Thus, it is easily understood that there are numerous clinical pictures that may be displayed by these patients in whom tumor function is not clean cut and limited to one of the foregoing main groups.

INCIDENCE

We will limit our discussion to the appearance of this tumor in children. During a 26 year period, 83,220 patients have been admitted to the Riley Hospital for Children. There have been 4 authenticated cases of adrenal cortical tumors, all of which proved to be carcinoma. Numerous other children showing variations of the adrenal cortical syndrome have been studied and either proved to be suffering from cortical hyperplasia or operation to ascertain the true identity of the lesion was refused.

Read at annual meeting, North Central Section American Urological Association, Milwaukee, Wis., October 13, 1950.

[1] Walters, W. and Sprague, R.: Ann. Surg., 129: 677, 1949.

[2] Cahill, G. F., Melicow, M. M. and Darby, H. H.: Surg. Gynec. & Obst., 74: 281, 1942.

[3] Kenyon, A. T.: Surgery, 16: 194, 1944.

[4] Cahill, G. F.: Surgery, 16: 233, 1944.

It is generally agreed that androgenic tumors with or without Cushing's syndrome are the most frequently encountered. These tumors occurring in children produce heterosexual changes in the female and isosexual changes in the male. The female child is more often affected. Those having purely metabolic features (Cushing's syndrome) are relatively rare as are those having no hormonal characteristics. The nonhormonal tumor is particularly rare among children. Estrogen-producing tumors either in male or female children are extremely rare. Cahill[2] reported one such case in an adult male.

DIFFERENTIAL DIAGNOSIS

Endocrine disorders arising in other sites must be excluded. As emphasized by Smith, Evans and Warkany,[5] two other sources of endocrine disease may give rise to confusing clinical states. Cerebral lesions in and about the pineal body as well as the hypophysis may be responsible for an excess production of adrenocorticotropic hormone or gonadotropic hormones which may produce precocious or pseudoprecocious puberty and thus mimic the primary adrenal cortical syndrome. Careful study of skull bony outline may detect a central lesion responsible for the clinical picture encountered. It is also well known that neoplasms of the gonads may produce hormones behaving functionally in a similar manner. A tumor of the gonad mimicking the adrenal cortical syndrome will usually be found on palpation although they may be quite small and escape detection.

Lesions of cerebral and gonadal origin having been excluded, differentiation of the lesions of the adrenal cortex may then be done in so much as is possible. Limitations in diagnosis are definite; surgical exploration may be imperative to establish the true identity of the lesion. Roentgenographic visualization of the adrenal overgrowth by perirenal air insufflation has been employed successfully. Pyelographic studies may disclose renal displacement on the affected side.

Modern methods of androgenic determination with fractionation into alpha and beta components together with estrogenic assay enable an increasingly accurate evaluation of tumor function. To these are added methods for laboratory evaluation of the electrolyte regulating, as well as carbohydrate, protein and fat regulating hormones. Determination of the 17-ketosteroids may be quite helpful. With the normal values of practically 0 mg. until the age of 7 years and the slow rise to adult levels from 7 years until puberty one may rather accurately detect gross androgen overproduction. Quantitative levels in the higher brackets seem to be largely the result of tumor whereas adrenal cortical hyperplasia seldom produces high levels. This is not always dependable, however. Fractionation of the ketosteroids into alpha and beta segments may give even more accurate information inasmuch as the cortical tumor produces a level composed of relatively more beta fraction than does the cortical hyperplasia. Escamilla[6] and many others have published data pertinent to this determination in clinical diagnosis.

As in case 1 the 17-ketosteroid level may not be elevated, while other steroids of metabolic significance may be considerably in excess of normal. Estrogen levels are elevated infrequently. Biochemical determination of the cortico-steroids, which regulate electrolyte balance, carbohydrate, protein and fat metabolism, is of value. Those patients displaying the Cushing syndrome will often show elevations of this fraction. The normal value in the child is thought to be between 0.3 and 0.4 mg. for a 24 hour urine sample.

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[5] Smith, P. G., Evans, A. T. and Warkany, J.: J. Urol., 64: 784, 1950.
[6] Escamilla, R. F.: Ann. Int. Med., 30: 249, 1949.

CASE REPORTS

Case 1. (S.O. XR 107461.) On March 6, 1947 a 2 year old white girl was admitted to this hospital, the parents complaining that the child weighed too much, had a recent excessive hair growth over the general body surface and wet herself at frequent intervals. The child had enjoyed normal health and development until 6 months prior to admission. At that time excessive weight gain was noted. A profusion of hair over the back, vulva and forehead made its appearance 2 months later. Acne developed 1 month prior to admission. Glycosuria and albuminuria were reported by the family physician. A prodigious appetite developed during the progression of the disease, as well as a noticeably increasing irritability. The mother described progressive polydipsia accompanied by increased bed and clothes wetting.

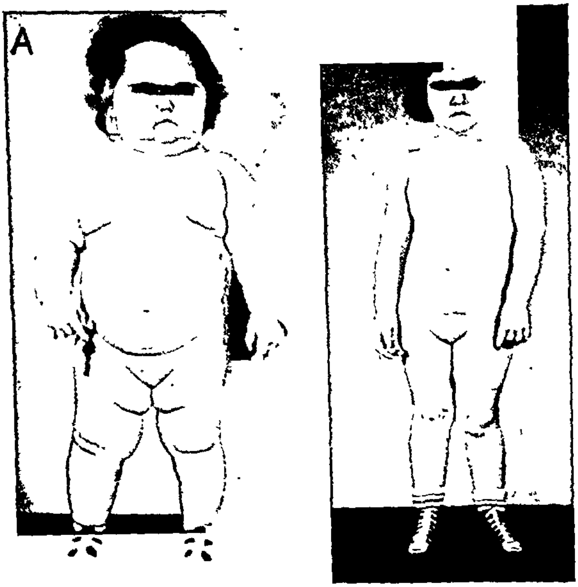

FIG. 1. Case 1. *A*, grotesquely obese 2 year old girl, preoperative. *B*, 2 years postoperative.

At examination a grotesquely obese child (fig. 1, *A*), weighing 41 pounds was seen. Coarse hirsutism over mons veneris and downy hair over the forehead, shoulders, back and legs were noted. There was a generalized facial acne. Hypertension of 180/120 was found. There were no detectable breast changes, nor was there hypertrophy of the clitoris. No masses could be palpated in the abdomen.

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One month after discharge, when seen in the follow-up clinic, the child appeared somewhat less excitable. Appetite had diminished and a weight loss of 1½ pounds was noted. The blood pressure recorded at that time was 120/80. A two-year follow-up was completed on June 4, 1949. The child's weight and appearance were normal (fig. 1, B) as was the blood pressure.

Case 2. (S.M. XR 11650.) A 2 year old white boy was admitted to the hospital on December 13, 1930 in a moribund state with multiple ulcerations over the extremities, abdominal swelling and the complaint of numerous nosebleeds. The child had been ill for 1 year. The first noted abnormality according to the parents was that of excessive weight gain.

Examination of the child demonstrated an excess of fat over the trunk, the extremities not participating. The cheeks were full and plethoric. Body weight was 28 pounds. Purpuric areas noted over the body apparently were not striae. The fontanel was open. It was recorded that the genitalia were well formed. There were numerous ulcers over both lower extremities. An excess of hair over the body was not localized.

Laboratory findings: white blood cells 4,700; red blood cells 4,600,000, bleeding time 35 minutes, clotting time 8 minutes, platelets 315,000. Differential showed 29 neutrophils, 55 lymphocytes, 1 eosinophil and 15 mononuclears. The urine was negative. No note was made of polyuria. Urinary hormonal studies were not done. Blood serology was negative.

X-ray studies of the long bones showed delayed ossification. The child's hospital course was rapidly downhill, in spite of numerous blood transfusions. During the entire hospital stay a temperature elevation of moderate degree was recorded. Ulcerations on the extremities increased in number and size, coalescing in some areas. The child died on its fourteenth hospital day.

Autopsy report: There was a disproportionately large amount of fat deposition over the trunk. Numerous hemorrhagic ulcerative areas were noted over the extremities and trunk. On opening the abdomen, the spleen and liver were uniformly enlarged. A tumor mass, weighing 70 gm. was found in the left adrenal bed. It was spherical and brownish-yellow in hue on section. Microscopic diagnosis of this tumor was carcinoma of the adrenal cortex. Several enlarged para-aortic lymph nodes were sectioned and found to contain deposits of metastatic carcinoma. The pituitary was carefully sectioned and found to be normal.

Case 3. (S.T. XR 14894.) A 4 year old girl was admitted to the Riley Hospital on December 18, 1931. The parent stated that a mass had been noted in the abdomen 1½ years previously which had progressively become larger. Marked growth of the clitoris had occasioned its removal 8 months previously. Voice changes had become prominent, lowering to an adult male level. An acne had existed for many months. No breast changes were noted. Vaginal bleeding had not taken place.

On examination the blood pressure was found to be 98/70. No note was made of obesity. The abdomen was markedly enlarged due to a tumor mass indefinitely outlined in the left flank (fig. 3). Labia were thought to be adult in size. Pubic hair was luxuriant and distributed in male fashion. Axillary hair was undeveloped.

Blood count: hemoglobin 11 gm., white blood count 15,850 of which 48 per cent were polymorphonuclears (no eosinophils). The fasting blood sugar on two occasions was 80 and 186 mg. per cent, total nonprotein nitrogen 34 mg. per cent, cholesterol 126 mg. per cent, serum potassium 22 mg. per cent (5.6 mEq.), serum sodium chloride 624 mg. per cent (106 mEq.), serum phosphorus 3.8 mg. per cent, serum calcium 13 mg. per cent and 4 plus cephalin flocculation. Survey films of the skull were normal. Ossification centers in the wrists were normal. Plain urograms on several occasions demonstrated a spherical soft tissue mass superior to the right kidney (fig. 2, *A*), which proved to be displacing the right kidney downward, rotating its long axis to the horizontal in the anteroposterior plane (fig. 2, *B* and *C*). The hypertension during the preoperative phase maintained its high level without wide fluctuation. Determination of the 24 hour urinary 17-ketosteroid output was found to be less than 1 mg. Unfortunately this was not repeated. Urinary estrogens and corticosteroids were not determined.

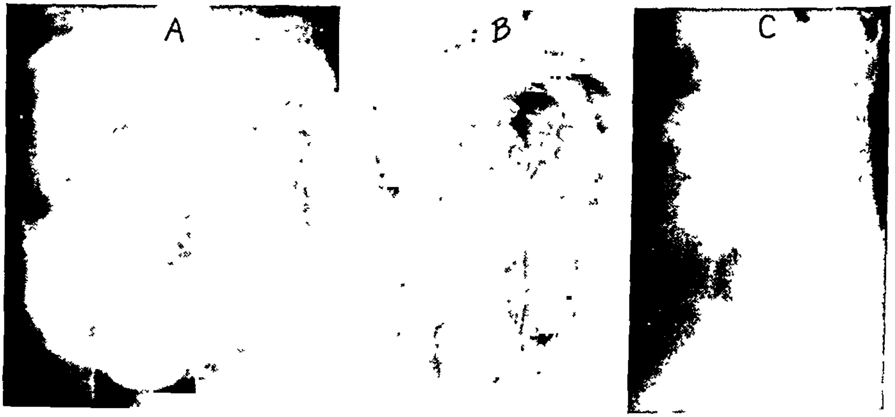

FIG. 2. Case 1. *A*, plain urogram showing spherical density above right renal outline. *B*, retrograde pyelogram (anteroposterior) showing downward displacement of right kidney. *C*, retrograde pyelogram (lateral) showing downward displacement and rotation of right kidney.

On the sixteenth hospital day, the child suffered a sudden episode of cyanosis. The pulse rose to 145 and the blood pressure to 200/160. Pulmonary congestion ensued and the patient appeared to be in acute left ventricular failure. The patient's general condition improved slowly under supportive measures.

A transperitoneal approach to the right adrenal was carried out on March 26. Palpation of the left adrenal gave the impression that this gland was normal. A tumor measuring 5 by 4 by 3 cm. was enucleated from the right adrenal bed. Pathologic study showed a highly cellular mass, the cells of which were polygonal and contained eosinophilic cytoplasm. Numerous mitotic figures were seen. A dense capsule embraced the neoplasm. The diagnosis of adrenal cortical carcinoma was made. The postoperative course was satisfactory. No cortical extract had been administered prior to surgery, however percortin was utilized for 24 hours immediately postoperatively. At no time did signs of adrenal cortical insufficiency develop. On the contrary the hypertension persisted steadily at 170/135. The child was discharged on the tenth postoperative day.

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Laboratory studies: red blood cells 5,080,000; white blood cells 17,300 with normal differential (no eosinophils); repeated urinalyses were normal; blood total nonprotein nitrogen was 38 mg. per cent. No hormonal studies were done on the urine. Barium enema indicated gross displacement of the descending colon to the right. No metastatic deposits were found in the chest or long bone studies.

A laparotomy was done January 12, 1932. A large encapsulated tumor mass 23 by 16 by 11 cm. was removed from the left adrenal fossa together with adherent overlying peritoneum. Histologically the picture was that of a highly cellular uniform mass of polyhedral cells resembling the cells of adrenal cortex. The diagnosis of carcinoma of the adrenal cortex was made.

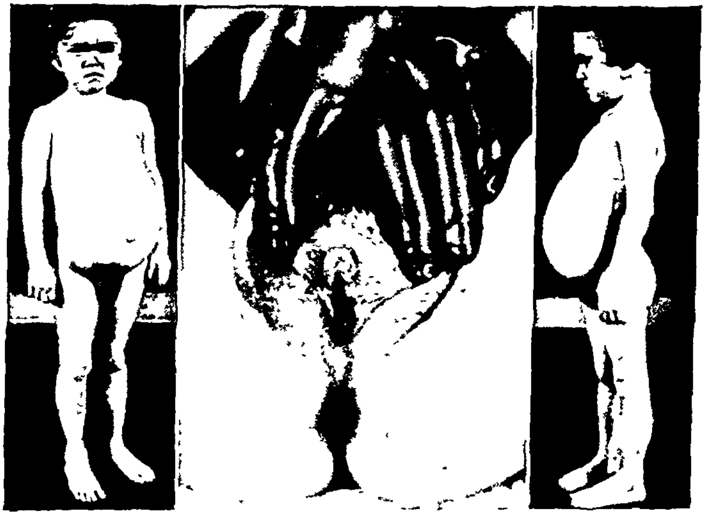

FIG. 3. Case 3. Showing abdominal distention due to tumor and hypertrophy of clitoris.

The postoperative course of the child was characterized by hyperpyrexia. No hormonal replacement therapy was given. The blood pressure fell to shock levels in spite of blood transfusions and supportive therapy. Vomiting became severe. The patient expired 36 hours after surgery. An autopsy was refused.

Case 4. (F.W.S. XR 144878.) A 12 year old boy was admitted on June 6, 1950 to the Riley Hospital with the complaints of obesity, growth of a beard and weakness. Approximately 1 year previously it was noted that the child, formerly quite extrovertive, came to prefer seclusion. He had no complaints. In January 1950, a rapid increase in weight took him to a physician who prescribed a reduction diet. At about the same time the boy began to grow a coarse black beard and pubic hair became luxuriant. These characteristics progressed unabated. In recent months fatigue and weakness became prominent. Pain in the abdomen made its appearance in May 1950. No polyuria or polydipsia was noted. The abdomen became quite distended during the 2 weeks preceding admission. Ankle edema simultaneously became pronounced. No acne has accompanied the illness. The past history was not significant. The family history was noncontributory.

On physical examination a very obese child was seen (fig. 4). The obesity was confined to the torso with little extremity involvement. There was a pronounced buffalo-hump formation. The head was almost spherical. Beard on the lip and cheeks was pronounced. A plethoric appearance was striking. Pubic hair was adult in distribution and quantity. Genital development approached that of an adult. Numerous purple striae were seen on the flanks and thighs. There was no palpable lymphadenopathy. The lungs were clear. The heart was normal to physical examination except for a moderate tachycardia of 100 beats. The blood pressure was 160/110. Abdominal examination revealed two distinct masses. One emerged from beneath the left subcostal margin to extend downward to the umbilicus and medially to the midline. It was rather immobile and painful, but smooth. The second, presumably liver, extended 6 cm. inferior to the right subcostal margin and was not nodular. The prostate, on rectal examination, was considerably larger than would be expected in a child of this age, although it was normal in all other respects. The neurological examination was negative. Blood count: hemoglobin 12 gm., red blood cells 4,250,000; white blood cells 10,900, bands 20, polymorphonuclears 66, lymphocytes 8, large monocytes 6. The urinalysis was repeatedly negative. The Randolph eosinophil count was 44. Blood serology for syphilis was negative. The blood nonprotein nitrogen was 31 mg. per cent. Blood sugar was 142 mg. per cent. Serum sodium was 143 mEq., potassium was 5.7 mEq. On two occasions the urinary 17-ketosteroids were 60.5 and 51.3 mg. per cent. Urinary gonadotropic hormones were at a low normal level. Estrogenic hormones in the urine were found to be greater than 20 r.u. per liter. Urinary corticosteroids were elevated to 3.5 mg. Roentgenographic survey included normal skull films. Bone age was found to be normal. There was no demonstrable osteoporosis. A plain urogram and excretory urograms revealed a large spherical mass in the left upper quadrant, stippled with amorphous calcific

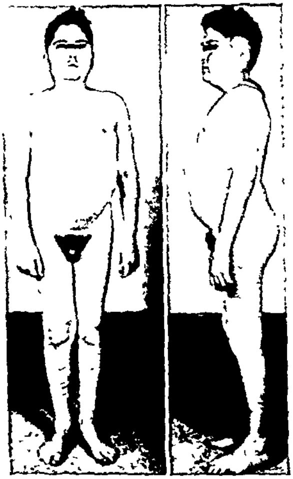

FIG. 4. Case 4. Showing typical facies of Cushing's syndrome. Note striae over thighs and legs, and adult pubic hair.

deposits, displacing the left kidney downward and laterally. Aside from gross displacement the pyelograms were normal.

The preoperative phase was uneventful. The child preferred to remain in bed most of the time. On June 22, 1950 a thoraco-abdominal approach was utilized. The large retroperitoneal mass, seemingly encapsulated yet quite fixed, was seen displacing the splenic flexure of the colon downward. Liver palpation disclosed three metastatic nodules varying from 5 to 15 mm. in diameter in the left lobe of the liver. It was felt futile to remove the primary tumor mass, so biopsy was taken and the abdomen closed in layers with silk sutures. The pathologic study showed solid sheets of polygonal cells having pink staining granular cytoplasm. There was considerable variation in nuclear size and staining properties although few mitoses were seen. Adrenal cortical carcinoma was advanced as the histologic diagnosis.

A trial of abdominal radiation 1 week after surgery precipitated increasing dyspnea and cyanosis. This was discontinued after little tumor response. Wound healing was slow and indolent. A downhill course characterized by increasing dyspnea, abdominal pain and loss of appetite terminated in death on September 3, 1950. No postmortem examination was obtained.

DISCUSSION

In attempting clinical classification of these cases, all but case 2 are susceptible of clean cut disposition. The presence of obesity, hypertension, hirsutism and acne without virilism in case 1 points to the pure Cushing's syndrome. The absence of 17-ketosteroid elevation in this child further strengthens this classification. Presence of the Cushing's syndrome with precocious virilism and elevation in the ketosteroid and corticosteroid levels place case 4 in the class of tumors displaying metabolic and androgenic features. Case 3 may be placed in the purely androgenic group in the presence of marked masculinization with absence of obesity and hypertension. The excessive body hair and obesity in case 2 suggests a purely metabolic tumor displaying Cushing's syndrome. However, the terminal state of this child and the incomplete workup make such a disposition questionable.

Many facets of hormonal imbalance are displayed by these cases. As is not infrequently found, the presence of excessive androgen and estrogen was found in case 4. Undoubtedly estrogenic effect was blanketed by a proportionately stronger androgen activity. Hyperglycemia was noted twice (cases 1, 4). This insulin resistant type of hyperglycemia is thought to be the result of excessive gluconeogenesis initiated by the hypercorticism. The presence of hypertension (cases 1, 4) is mediated by an uncertain mechanism. It is interesting to note the persistence of hypertension for at least 10 days after complete removal of the tumor in case 1. We misinterpreted this fact to indicate distant functional metastases. The urgency of surgery in the pronounced hypertensive patient is illustrated in case 1, where acute cardiac failure supervened, and was corrected only with difficulty. While it is well known that sodium and potassium metabolism are directly influenced by adrenal cortical activity it is notable that serum levels of these electrolytes are infrequently abnormal in adrenal cortical tumors.

Aberrations in electrolyte balance in such cases are best detected by sweat and urine excretion values. Polyuria, a primary complaint in case 1, is apparently due to direct action of an adrenal cortical diuretic substance upon renal tubular epithelium. The overproduction of this hormone, normally acting in balanced interplay with pituitary antidiuretic hormone, upsets water balance.[7]

X-ray studies may be decisive in diagnosis. Pyelographic studies disclosed renal displacement in cases 1 and 4. The mass may be quite visible on flat plate of the abdomen (cases 1, 3, 4).

The transperitoneal approach to the adrenal through a transverse abdominal incision has seemed satisfactory in our hands. It allows simultaneous exposure of both adrenals through one incision as well as general visceral palpation for metastases. An exceptionally large tumor may be exposed to advantage by the combined thoraco-abdominal approach (case 4).

Postoperative management is of vital importance, particularly in those children displaying Cushing's syndrome. Acute adrenal insufficiency may occur after removal of these tumors (case 3). Frequently partial atrophy of the contralateral adrenal may co-exist. Thus, transitory insufficiency until resumption of full function of the atrophic gland may be adequately handled with the judicious use of adrenal cortical extract, desoxycorticosterone acetate and saline infusions.

Prognosis depends to a great extent upon the type of tumor encountered. Nonfunctional tumors, of course, often manifest themselves by mass alone. This is frequently too late for surgical extirpation. Simple estrogenic and androgenic tumors are susceptible of early detection. Their surgical removal is seldom accompanied by acute adrenal insufficiency, although this apparently occurred in case 3. Those tumors having "cushingoid" characteristics while often discovered early, may have a fatal outcome if acute adrenal insufficiency following surgery is not skillfully managed.

The salvage of only one of the 4 patients here reported emphasizes the great need for early diagnosis and aggressive postoperative treatment. All three cases with fatal outcome should have been recognized earlier. Adequate postoperative hormone administration will greatly reduce the mortality attributable to adrenal insufficiency.

SUMMARY

Four cases of adrenal cortical carcinoma in children are reported.

A brief discussion of a classification based upon functional activity of these tumors is presented.

The differentiation of these lesions from similarly functional states related to cerebral or gonadal origin must be made.

The variable clinical modes of manifestation may be explained on the basis of steroid physiology.

The author wishes to acknowledge with gratitude the use of "Pediatric Urology in Indiana University, Abstracts of Clinical and Autopsy Records from 1924 to Date" by Drs. H. O. Mertz and Frank Forry, in the preparation of this paper.

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[7] Lotspeich, W. D.: Endocrinol., 44: 314, 1949.

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Vol. 66, No. 4, October 1951
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DOUBLE KIDNEY: REVERSAL OF THE WEIGERT—R. MEYER LAW: A CASE REPORT

E. C. ST. MARTIN, H. A. O'BRIEN AND J. D. MITCHELL

The upper half of a double kidney with a duplicated ureter enters the bladder caudal and medial to the orifice of the lower half, with such consistency (the Weigert—R. Meyer law), that any reversal of this picture is worthy of reporting. Lund recently reported this condition, plus the presence of uncrossed ureters. His case was the third reported in the literature, where the orifice from the upper renal segment was cranial and medial to the orifice of the lower segment. The embryology and literature were covered, and nothing need be added with this report.

CASE REPORT

A 36 year old Negro was referred to us because of total, painless hematuria of 7 days' duration. With the usual vagueness of information obtainable from this man's race, the patient made it difficult to secure a coherent history. After piecing several versions of the sequence of events, this conclusion was reached.

About a month previously, he was beaten in a fisticuff, his lumbar areas being trampled for good measure. He experienced hematuria for 24 hours. Two and a half weeks later, he became quite intoxicated on "white mule whiskey." He passed out and admits being given vigorous artificial respiration by his friends, probably another trampling. This was followed by acute gastritis and recurrence of the hematuria. The former subsided under the usual carminatives and antispasmodics. However, the hematuria persisted, and cystoscopy by his rural physician revealed "blood coming from both orifices." The previous genitourinary history was negative except for a Neisserian infection 15 years before admission.

He was transferred to our care at this time, July 27, 1949. He was a well developed, well nourished Negro, who appeared dehydrated. His pulse was 92 and his blood pressure was 140/75. There was a definite pallor of the conjunctiva. No bruises or masses were present in the lumbar area, but he complained of soreness in the costovertebral angle. The urine was wine colored and loaded with red blood cells.

Excretory urograms revealed bilateral double kidneys. The renal shadows were large but equal in size. There were no fractures and no extravasation of dye. A tentative diagnosis of "contusion of the kidneys" was made. He was placed on absolute bed rest. Penicillin was started because of low-grade fever. Vitamin K and Rutin were tried although the bleeding, clotting, and prothrombin times were normal. There was no sickling of his red blood cells. Blood transfusions were given, the hemoglobin being 10.5 gm. after 1000 cc of blood. The blood urea was normal.

The hematuria decreased in intensity daily. By August 1, 1949, the urine was almost clear. The tentative diagnosis was still traumatic hematuria. Despite the spontaneous clinical improvement, completion of the urological investigation was believed to be indicated. Under spinal anesthesia, cystoscopy was done. Blood tinged urine spurted from a small ureterocele on the left. Two catheters were inserted into the left orifice with the hope that each would ascend a separate ureter Blood tinged urine flowed from one catheter. Specimens were collected for study, and retrograde pyelograms were made. Two ureteral orifices of unusual relative position were found on the right. The efflux was clear from both. Then

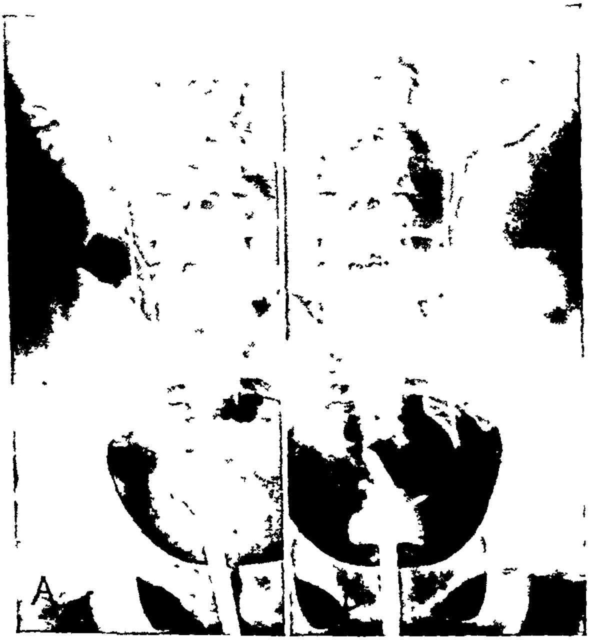

Fig 1

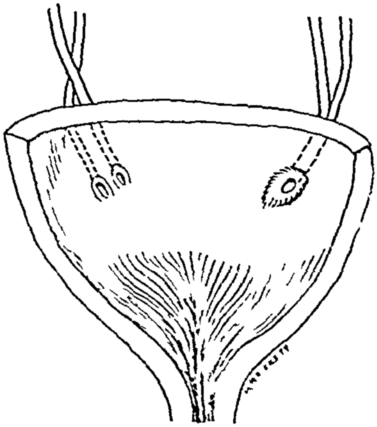

Fig. 2

catheters were inserted up the two right ureters with clear urine being collected. Retrograde pyelograms (fig. 1) revealed that the bloody urine was coming from the upper half of the left kidney. There was no deformity of either pelvis, but a Papanicolaou stain was made. This was negative. The ureters joined near the ureterovesical junction (fig. 1, *B*).

On the right side, the catheter going into the upper orifice went to the upper half of the kidney (fig. 1, *A*). The orifice was definitely above and medial to the orifice of the lower half (fig. 2).

Two days later, the urine was grossly clear. After the urine had been clear for 4 days, the patient was discharged on August 6, 1949. Eight weeks later, he returned for re-examination. He was asymptomatic. His urine (centrifuged) contained a few pus cells but no red cells. The pyelogram of the upper half of the left kidney was repeated and again found normal. The relationship of the two orifices on the right was again checked and found to be definitely as illustrated. The patient was advised to return in 6 months for routine examination.

COMMENT

Another exception to the Weigert—R. Meyer law is presented. Of additional interest was the hematuria. The etiology of the hematuria was concluded to be traumatic in origin. Drug sensitivity and bleeding due to alcoholic damage of the kidneys were considered. The finding of hematuria in only one of the pelves suggested the Papanicolaou stain. This was negative, as well as the repeated pyelogram.

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REFERENCE

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SURGICAL CONSERVATION OF RENAL PARENCHYMA

RUSSELL B. ROTH, ELMER HESS AND ANTHONY F. KAMINSKY

It is occasionally obligatory for the urological surgeon to cut into or partially resect a solitary kidney. Somewhat less frequently it may be mandatory to carry out secondary or tertiary operations upon solitary kidneys. Whatever may be the circumstances dictating such potentially perilous procedures, one feature is common to all: the necessity for maximum conservation of renal parenchyma.

In our clinic, over a period of years, we have repeatedly faced this problem, and have developed a profound respect for a kind Providence which bestows upon most men a four-fold abundance of functioning renal tissue. There are times when we may carry out nephrectomy for renal disease, confident that a normal contralateral kidney is more than adequate to maintain health. But when confronted by a single kidney, or a mere fraction of a kidney or bilaterally diseased kidneys, our surgery becomes a matter of salvage rather than sacrifice. The paramount problem becomes one of hemostasis.

Many ingenious methods for hemostasis and renal suturing have been devised, in recognition of the friability of renal substance. Foremost among these have been methods utilizing the capsule, though the capsule itself may shred and tear in a most discouraging fashion. Second in popularity would seem to be the utilization of fat or muscle pads under the extrarenal portions of the sutures, to prevent cutting. Ribbon catgut has been used because of its minimal tendency to lacerate. But when one depends on hemostatic sutures one depends on producing ischemia and infarction in at least a portion of the renal tissue left behind. It would be far superior if one could, with safety, dispense with sutures altogether.

In a small number of cases wherein it appeared important to salvage every scrap of available renal parenchyma we have had the temerity to do without suturing the kidney, depending for hemostasis upon the maintenance of approximation of the cut portions of the kidney by a wrapping of oxycel. In the cases in which we have used it, it has proven thus far to be a feasible procedure.

Our concern here is with a method of applying sufficient pressure to control hemorrhage without so constricting the kidney substance as to cause infarction and tissue destruction. In practice this has been achieved in the following manner.

When the kidney is split longitudinally, after the required procedures have been carried out, the two halves are apposed as accurately as possible and so maintained by gentle manual pressure. Assuming a normal clotting time of 3 minutes, this gentle manual compression is maintained for 5 minutes to give a small margin of safety. Moistened sheets or strips of oxycel are then snugly wrapped about each pole of the kidney to maintain this apposition. The kidney is carefully replaced in its fossa and the patient is dropped out of lateral extension by having the kidney elevator lowered. The kidney is then observed for several more minutes to assess the adequacy of hemostasis. Closure is made in the usual

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Read at meeting, Northeastern Section, American Urological Association, Bolton Landing, N. Y., September 14, 1950 fashion, with or without drainage as the circumstances may demand, but in our practice almost always with a Penrose drain brought out through the posterior angle of the incision.

When resection of a pole of the kidney has been performed the incisions are made so as to remove a wedge of parenchyma, but even then it is rarely possible to bring the cut surfaces of the remaining kidney into apposition without the use of sutures. Here it is our practice to roll back capsule over the area to be sacrificed, and, after excision of the required parenchyma, a pad of fat or a pledget of oxycel is pressed into the defect and held there for 5 minutes. The capsule is rolled back over the defect and oxycel sheets are wrapped about the kidney, longitudinally to maintain the mild pressure. The kidney is replaced and watched as mentioned previously.

There can be no quarrel with the surgical axiom which says that accurate clamping and ligation of bleeding vessels is of primary importance. But this is not an axiom which is applicable to incision of the renal parenchyma save in that rare combination of circumstances wherein there is extrarenal branching of the renal artery, and compression of appropriate branches happens to make ischemic that portion of the kidney which one wishes to excise. Under such circumstances the matter of hemostasis becomes immensely simplified. The proper vessel is ligated and the resection is done within the ischemic area. More generally there is no such opportunity to render the field relatively bloodless. One must rely on temporary occlusion of the renal pedicle while the work is being done. Those who use modifications of a tourniquet, or rubber shod clamps, may be upon safe ground, but it has been our practice to rely on compression of the renal pedicle between the index and middle finger of the left hand, or between the fingers of an assistant. Compression can be achieved with the least practical force and a minimum of trauma to the vessels. With adequate exposure of the kidney this is rarely a clumsy or inconvenient procedure, save when the pedicle is extraordinarily short.

We do not need to belabor the point that the brisk bleeding which is encountered upon incising renal parenchyma cannot be controlled by clamping and tying, nor is it practical to attempt fulguration. One must incise as required and rely on pressure principles afterward to stanch the hemorrhage. It is possible to split a kidney from pole to pole for purposes of removing large calculi or exploring the renal substance. The two halves may then be reapposed, held firmly in position, and satisfactory hemostasis may be achieved. Urological surgeons in particular are familiar with the reliability of pressure on the cut ends of vessels, since so many rely upon it for control of hemorrhage in prostatic enucleations or resections.

Oxidized cellulose gauze, soon after its preparation by Kenyon, was seized upon by urologists because of its nontoxic hemostatic properties. Fish, in 1946, reported its use in a series of cases including 16 instances of renal surgery, wherein the gauze was held in apposition to the bleeding surfaces. He also suggested that "a ruptured kidney could be handled in the same way and it is conceivable that rather badly damaged kidneys might be repaired with the hemostatic gauze."

There are numerous other reports of the use of the gauze in renal surgery, notably by DeVries and Buchanan, and by Goldstein and Hollander. The latter authors report one instance of hemorrhage 28 hours postoperatively necessitating reopening of the incision. In all cases it appears that the gauze was used much as fat or muscle pads had previously been used, to secure pressure hemostasis, plus the utilization of the intrinsic hemostatic effect of the oxidized cellulose. In no instance does it seem to have been used in lieu of suture material.

Oxidized cellulose gauze, when saturated with blood, rapidly softens and loses its tensile strength, hence there is little question of undue constriction of renal substance by this method. There may, on the other hand, be question as to whether or not we are deluding ourselves into believing that oxycel maintains any apposition at all. It is true, primarily, that intra-abdominal pressure maintains the apposition once the kidney has been replaced in its fossa, the incision closed, and the patient returned to a supine position. It is also true, however, that oxidized cellulose, after being exposed to blood, swells in volume and when tested in several layers, seems to maintain a fabric form for a matter of hours before changing into an amorphous mass. It is our conviction that wrapping with the gauze does assist in maintaining apposition.

ABSTRACTS OF THREE ILLUSTRATIVE CASES

Case 1. J. M., a 39 year old white man, was admitted to Hamot Hospital on March 3, 1949 with acute left renal colic. Examination showed two calyceal calculi in the right kidney and two calculi in the left, one of which occupied a lower minor calyx and one of which had become free in the pelvis and was obstructing the ureteropelvic junction (fig. 1). Operation was performed at which time the lower calyceal calculus was removed by calycectomy and the obstructing stone in the pelvis was also removed. Oxycel was used for hemostasis and in lieu of sutures to preserve a maximum amount of renal substance because of the bilateral disease. The patient made an uneventful recovery. The wisdom of preserving all possible renal parenchyma has since been proven, because on April 29, 1949 one of the right renal calculi became obstructive, (fig. 2) necessitating right pyelolithotomy. The second calculus could not be obtained at this operation but postoperatively the patient developed multiple renal abscesses with high temperature and extreme toxicity, so that nephrectomy was performed as an emergency life-saving procedure. The patient is now living comfortably, with a normal blood chemistry, on the remaining portion of the left kidney, although it must be noted that there is a small calculus in this kidney which is apparently being satisfactorily controlled by diet plus amphojel therapy, and there is radiologic evidence that the calculus has been reduced in size and density over the period of the last 12 months. There has been a persistent infection with B. pyocyaneus which is under therapy with terramycin.

Case 2. S. K., a 40 year old white female school teacher, was first seen by us in 1946 with constant severe right flank pain and a story of having had staghorn calculi previously removed from both kidneys. Study showed bilateral recurrent staghorn calculi. On December 6, 1946 the right kidney was exposed and split fashion, with or without drainage as the circumstances may demand, but in our practice almost always with a Penrose drain brought out through the posterior angle of the incision.

When resection of a pole of the kidney has been performed the incisions are made so as to remove a wedge of parenchyma, but even then it is rarely possible to bring the cut surfaces of the remaining kidney into apposition without the use of sutures. Here it is our practice to roll back capsule over the area to be sacrificed, and, after excision of the required parenchyma, a pad of fat or a pledget of oxycel is pressed into the defect and held there for 5 minutes. The capsule is rolled back over the defect and oxycel sheets are wrapped about the kidney, longitudinally to maintain the mild pressure. The kidney is replaced and watched as mentioned previously.

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lengthwise. The stone was removed and the kidney was repaired by wrapping with oxycel. The kidney functions well, blood chemistry values are normal, and the patient remains comfortable in spite of stone recurrence. The growth of the recurrent calculus has been rather dramatically controlled by the use of diet and amphojel therapy.

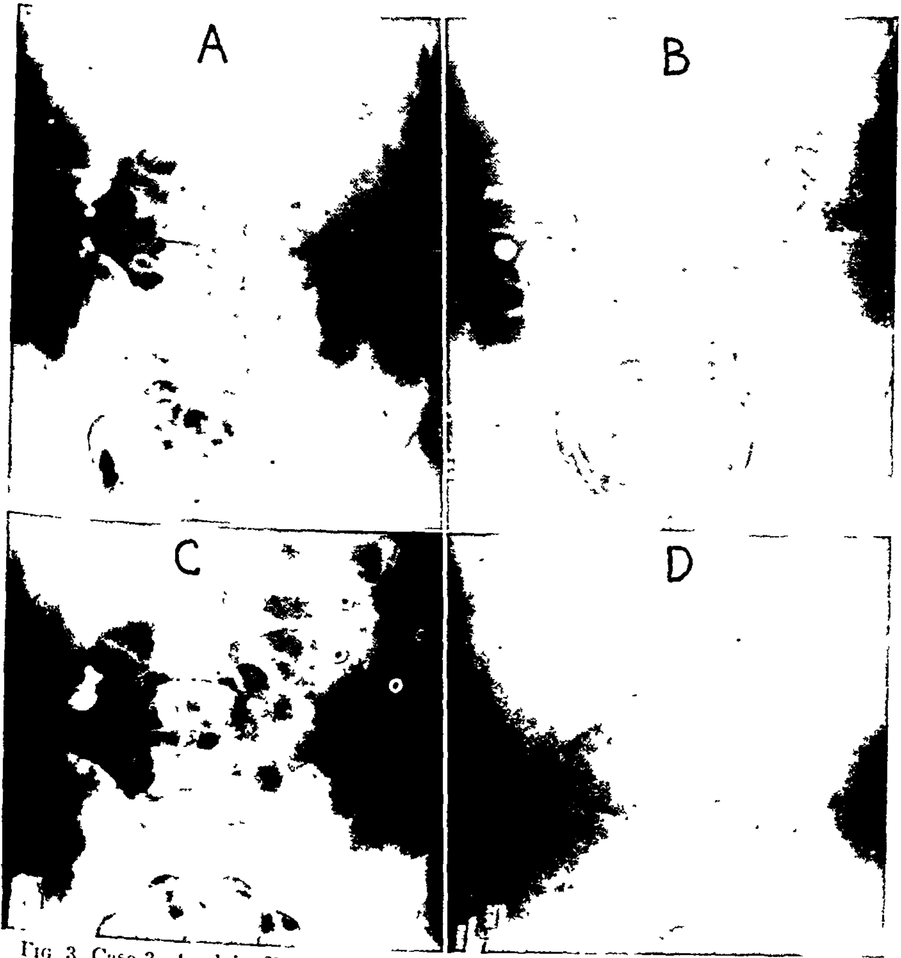

FIG 3. Case 3. *A*, plain film showing right calculous pyonephrosis and lower calyceal calculus on left. *B*, retrograde pyelogram of same *C*, plain film after resection of lower left calyx. *D*, excretory urogram after right nephrectomy showing status of solitary left kidney.

Case 3. M. S., a 42 year old man, was admitted to the urological department of St. Vincent's Hospital on August 11, 1949 complaining of right flank pain. He was found to have multiple large calculi and a calculous pyonephrosis on the right, but also a lower calyceal calculus on the left (fig. 3). The first operation was performed on August 12, 1949 removing the lower calyceal calculus by calycectomy Sutureless repair of the kidney was carried out by wrapping

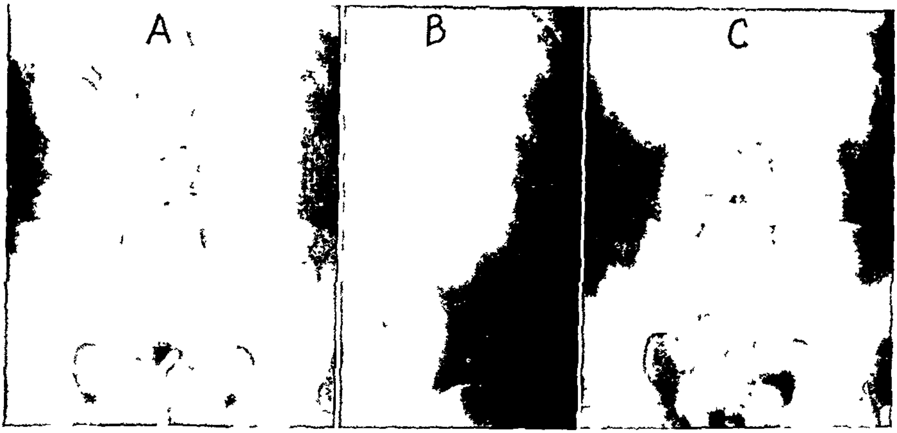

FIG. 1. Case 1. *A*, two right calyceal calculi and two left calculi, one of which was obstructive *B*, preoperative plain film of left kidney. *C*, postoperative excretory urogram after removal of lower calyx and removal of stone from left pelvis

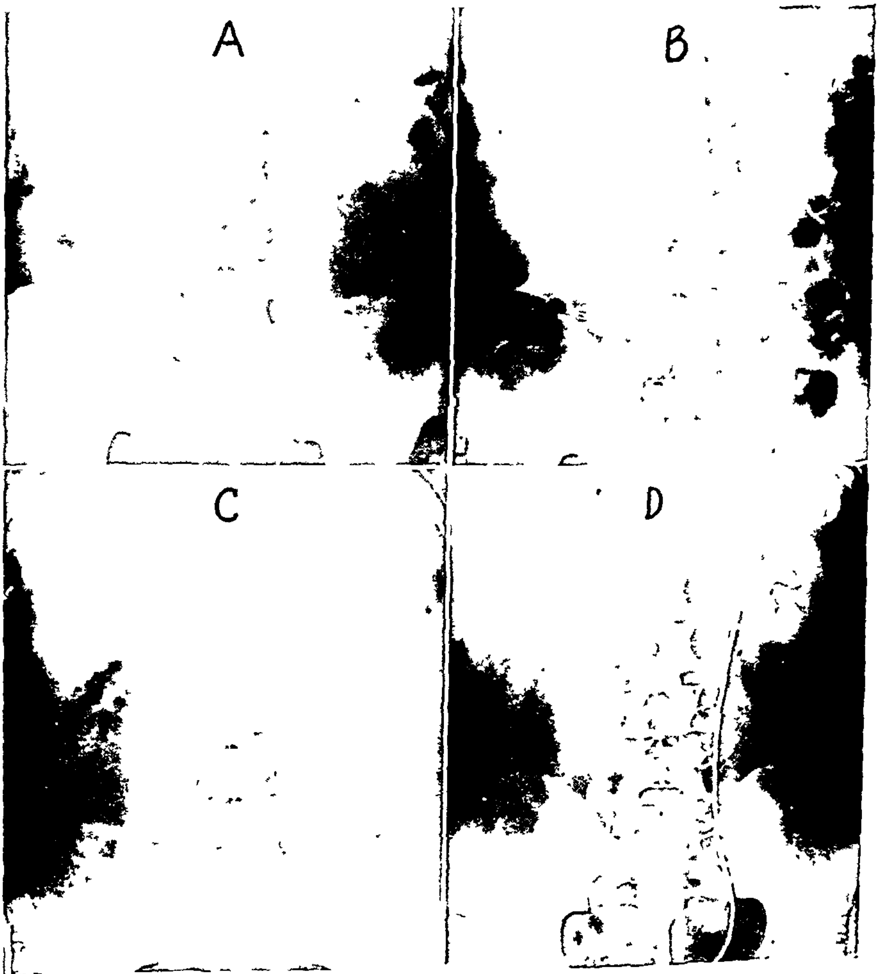

FIG 2 Case 1 *A*, one of right renal calculi obstructing ureteropelvic junction requiring removal *B*, similar obstruction by second calculus leading to removal of kidney with multiple abscesses *C*, postoperative plain film *D*, retrograde pyelogram of solitary remaining kidney

lengthwise. The stone was removed and the kidney was repaired by wrapping with oxycel. The kidney functions well, blood chemistry values are normal, and the patient remains comfortable in spite of stone recurrence. The growth of the recurrent calculus has been rather dramatically controlled by the use of diet and amphojel therapy.

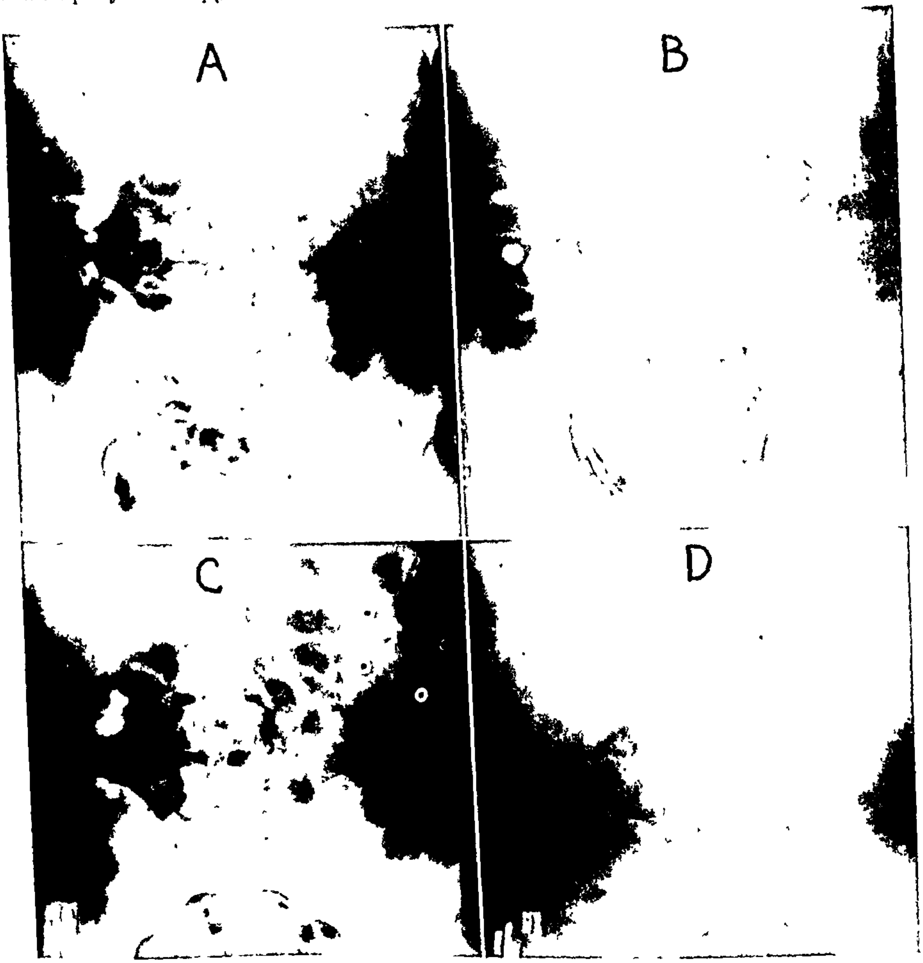

FIG. 3 Case 3 *A*, plain film showing right calculous pyonephrosis and lower calyceal calculus on left *B*, retrograde pyelogram of same. *C*, plain film after resection of lower left calyx. *D*, excretory urogram after right nephrectomy showing status of solitary left kidney.

Case 3. M. S., a 12 year old man, was admitted to the urological department of St. Vincent's Hospital on August 11, 1949 complaining of right flank pain. He was found to have multiple large calculi and a calculous pyonephrosis on the right, but also a lower calyceal calculus on the left (fig. 3). The first operation was performed on August 12, 1949 removing the lower calyceal calculus by calycectomy Sutureless repair of the kidney was carried out by wrapping with oxycel gauze. After an uneventful recovery, right nephrectomy was done 1 week later. The patient has been in good health since this time.

SUMMARY

In instances of bilateral renal disease, or when operating on a solitary kidney, it is often mandatory to salvage as much renal parenchyma as is possible. Sutures which compress and destroy remaining kidney tissue are therefore undesirable. It has been found feasible to avoid the use of sutures by employing pressure principles of hemostasis augmented by wrapping of the kidney with oxidized cellulose gauze to assist approximation of cut surfaces of renal parenchyma. Three illustrative cases are presented.

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REFERENCES

DeVries, J. K. and Buchanan, R. W.: J. Urol., **57**: 816, 1947.
Fish, G. W.: J. Urol., **56**: 375, 1946.
Goldstein, A. E. and Hollander, A.: J. Urol., 59: 105, 1948.

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RENAL ROENTGENOSCOPY AND ROENTGENOGRAPHY DURING SURGERY

R. J. PRENTISS AND R. B. MULLENIX

Fluoroscopy and roentgenography of the kidney during nephrolithotomy and pyelolithotomy are helpful, and at times, indispensable in the location of elusive calculi or fragments thereof. The kidney-holding clamp devised by Sutherland[1, 2] greatly reduces the difficulty of using these diagnostic aids. The clamp is essentially a bivalved instrument, each blade of which consists of a shell of thin aluminum hammered to kidney shape. The handles are inseparably joined by a spring which holds the clamp in the open position but permits approximation of the blades to enclose the mobilized kidney.

Since the instrument has not previously been produced commercially it has not come into general use and has never received the approbation to which it is entitled. We have now arranged for its manufacture, incorporating modifications which we believe increase the usefulness and flexibility of the instrument.

MODIFIED SUTHERLAND KIDNEY CLAMP

The size of the Sutherland clamp at times makes difficult its introduction into the wound and its application to the kidney. We have eliminated this shortcoming by making the blades of the clamp readily separable, making possible the application of each half individually, subsequently joining and securing the handles with a specially designed hinge-type locking device. This procedure resembles the introduction and application of individual blades of an obstetrical forceps.

The use of an aluminum shell completely enclosing the kidney renders difficult the introduction of needles into the kidney with the clamp in place, makes impossible any exploration of the kidney without removal of the clamp and may complicate the removal of the clamp without first withdrawing the localizing needles from the kidney. A cut-out aluminum shell is substituted resulting in a frame-work of thin aluminum strapping conforming to the shape of the kidney. Although retaining the kidney as firmly in the clamp, this design permits wide manipulation of the kidney through the large fenestrations in the shell (fig. 1).

METHOD OF USE

Following satisfactory exposure and mobilization of the kidney and following removal of readily accessible calculi, the kidney, if deliverable, is placed within the clamp or the clamp may be introduced into the incision and applied. Facilities permitting, fluoroscopy may first be performed following which radiographs are made. Both procedures are carried out in two projections to permit tri-dimensional localization. If necessary, needles are introduced into the kidney to facilitate localization of the calculus. A 10 by 12 inch cassette, protected by a sterile pillow case or towel, is held at the patient's back and the kidney held firmly in

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[1] Sutherland, C. G.: J. Urol., 33: 1-11, 1935.

[2] Sutherland, C. G.: Surg. Clin. N. Amer., 19: 1041-1046, 1939.

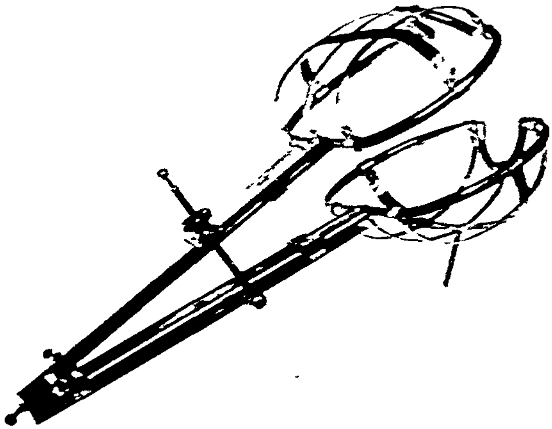

Fig. 1. Sutherland kidney clamp. Modified by Prentiss and Mullenix

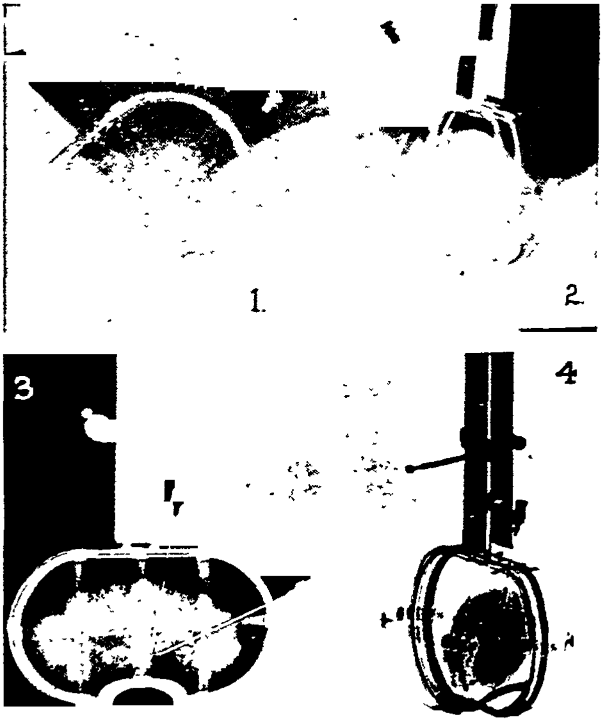

Fig. 2. Modified Sutherland clamp in use. *1*, Operating room film, projected at right angle to long axis of kidney. *2*, Operating room film, kidney rotated to facilitate localization of calculus. *3*, Demonstration film, excised kidney, similar to 1. *4*, Demonstration film, excised kidney, similar to 2.

the clamp during exposure. The relation to the film of the long axis of the kidney is altered by rotating the clamp (fig. 2).

SUMMARY AND CONCLUSIONS

Renal roentgenoscopy and roentgenography are invaluable aids in the location of elusive calculi or fragments thereof during nephrolithotomy and pyelolithotomy.

Renal injury is reduced by eliminating prolonged and damaging search for calculi.

Roentgenograms so produced offer medico-legal protection in cases of stone recurrence following surgical removal.

A suitable kidney clamp has been devised and manufactured. The Sutherland clamp has been modified and improved by making separable its two blades and providing wide fenestrations in the aluminum kidney-retaining shell.

The improved kidney-holding clamp outlines and fixes the kidney during fluoroscopy and roentgenography and, in addition, may be used as a kidney tractor in a wide variety of renal operations.

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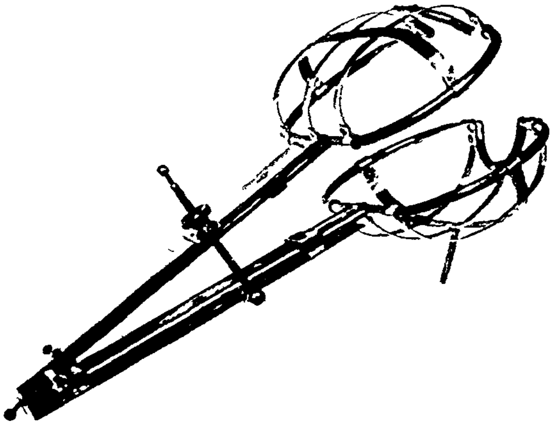

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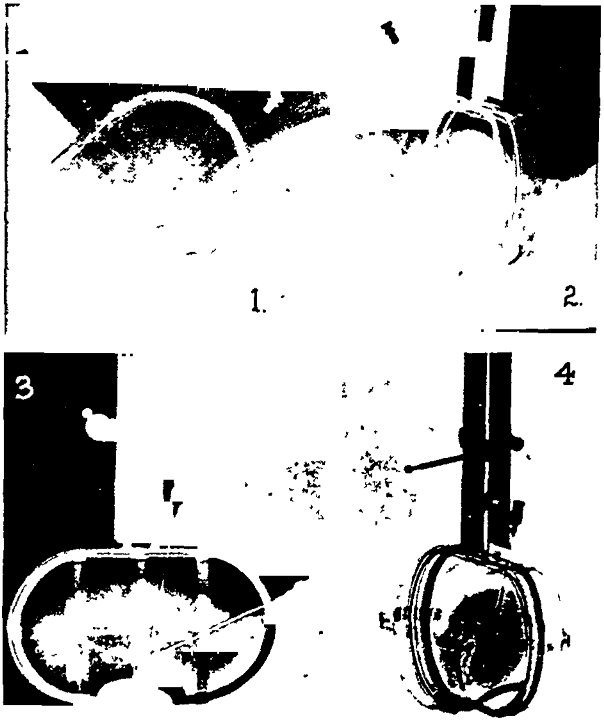

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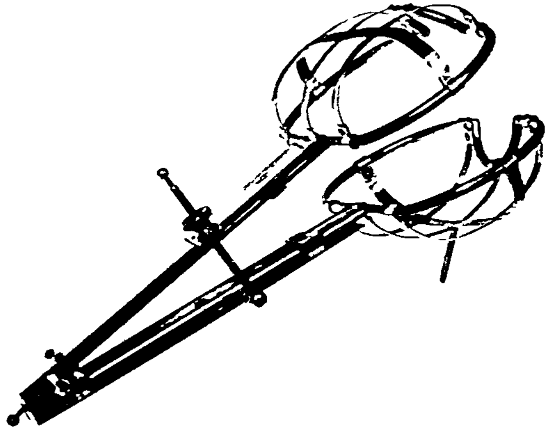
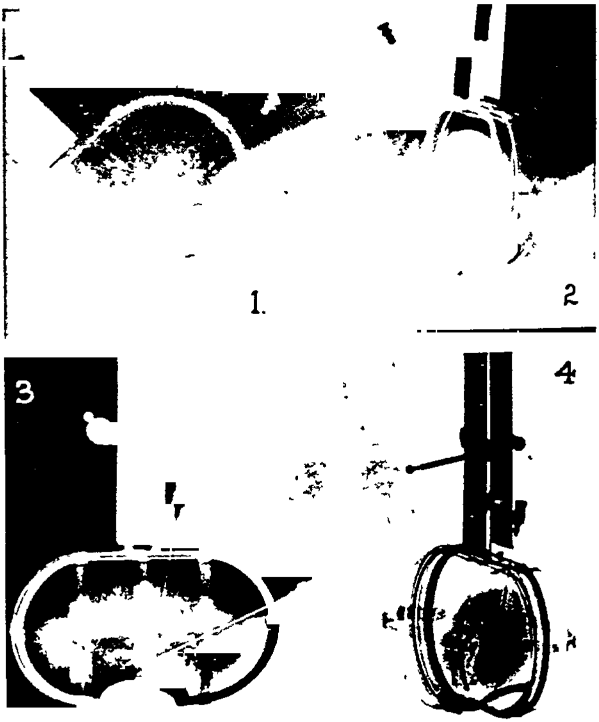


Fig. 1. Sutherland kidney clamp Modified by Prentiss and Mullenix



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SURGICAL RESECTION OF A TUBERCULOUS KIDNEY

J. ROBERT RINKER

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Surgical resection of the diseased portion of a kidney is a valuable procedure in several nontuberculous conditions where at least half of the kidney is free from disease and can be salvaged. Textbooks have long listed tuberculous involvement of the kidney as a contradiction to the procedure and justly so; but the advent of streptomycin has changed the prognosis in some cases of renal tuberculosis in which we formerly would have made dogmatic predictions as to their incurability. When the effectiveness of streptomycin in healing these lesions was established it became apparent that the belief that "tuberculous involvement was a contradiction to resection of the kidney in all cases" would have to be re-evaluated with streptomycin coverage and I began to watch for a case in which it would be suitable to try; consequently, this is an early report of an initial experience.

In a rather extensive review of the literature we have not been able to find a case report of a cure, or an unsuccessful result following resection of the tuberculous kidney, but it must have been tried as there are several statements condemning the procedure, though it could have almost been condemned on the basis of past knowledge of the disease without clinical trial.

Criteria for selecting a case for the procedure were first that the patient's lesions were such that standard acceptable procedures could not be applied with hope of cure, second, the only chance of cure being resection of a localized lesion too large to heal with drugs in a solitary kidney, in which the remaining portion of the kidney was pyelographically normal.

CASE REPORT

A 43 year old man had complete destruction of the right kidney due to tuberculosis (fig. 1, *A*). The left kidney had a large cavitating lesion of the lower pole with the remainder of the kidney pyelographically negative (fig. 1, *B*). The bladder showed tuberculous ulceration with slight reduction in capacity. Both ureters were involved in the lower third. Urine from both kidneys and bladder were positive for tubercle bacilli on direct smear, culture and animal inoculation. The patient received 1 gm. streptomycin daily for 62 days prior to a resection of the lower pole of the left kidney on September 12, 1949. On October 29 a right nephro-ureterectomy was done. Streptomycin and PAS were continued during and after the operation. Urine specimens taken at monthly intervals for concentrate, culture and animal inoculation were reported positive September 28, October 18, November 22 and December 6, 1949. The first negative was reported January 3, 1950. The urine was still negative October 3, 1950.

The urine remained positive for 6 weeks after the last surgical procedure and was, no doubt, the time required for the bladder and left ureter to become negative. There was marked contraction of the bladder on healing. Frequency due to decreased bladder capacity is the patient's only complaint at this time. We chose to do the resection of the kidney first because the possibility of operative mortality was calculated to be greater following heminephrectomy than nephro-ureterectomy. Had the patient survived nephro-ureterectomy, if it had been done first, then died after heminephrectomy, he would have been subjected to 2 operations instead of one.

If we are to rehabilitate the patient with genito-urinary tuberculosis, every attempt must be made to heal or remove all active lesions. That not only improves the patient's chances of recovery, but is also necessary before he can return to a normal life without the hazard of infection to others. Some minimize the danger of the patient with genito-urinary tuberculosis as a public health menace, but I personally know of a small child who died of tuberculous meningitis in a home where the father, who had genito-urinary tuberculosis, returned from a hospital against medical advice.

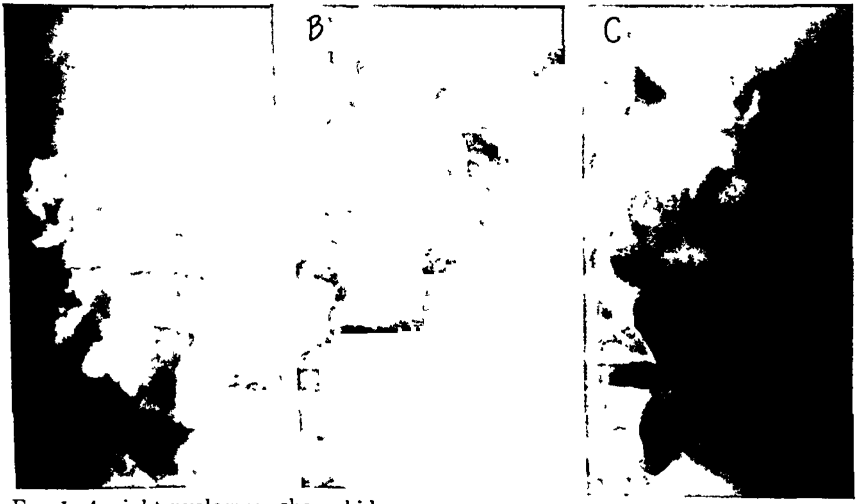

FIG 1 *A*, right pyelogram shows kidney completely destroyed by tuberculosis. *B*, cavitating tuberculous lesion involving lower pole of left kidney. *C*, postoperative left excretory urogram.

SUMMARY

A case is presented of a patient who had bilateral renal tuberculosis with complete destruction of the right kidney and a cavitating lesion of the lower pole of the left kidney, the remaining portion of the left kidney being pyelographically negative for the tuberculosis. With preoperative and postoperative streptomycin therapy, the diseased area of the lower pole of the left kidney was resected and nephro-ureterectomy was done on the right side. Urinalyses are repeatedly negative 12 months following resection of the tuberculous area of the left kidney, and the bladder has healed.

Addendum: The urine was still negative October 3, 1950.

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REFERENCE

RINKER, J. R. Clinical response of the tuberculous ureter to streptomycin therapy. J. A. M. A., 142: 87-89, 1950.

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TOTAL INFARCTION OF THE KIDNEYS FROM BILATERAL ARTERIAL EMBOLI

THOMAS F. KAISER AND RAYMOND R. ROSS

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The anuria accompanying total bilateral renal infarction from arterial emboli may be puzzling to the clinician. It is not the purpose of the authors to indulge in a discussion of the causes and differential diagnosis of anuria, but rather to emphasize an obscure entity of which the urologist should be aware.

Total infarction of the kidneys from bilateral arterial emboli is rare. Hoxie and Coggin[1] in reporting 1 case in 1940 reviewed 14,411 autopsies and failed to find a similar instance of this condition, although 205 of the post-mortem examinations in their large series showed some degree of renal infarction.

Bilateral total infarction does not always occur simultaneously as in the cases reported by Hoxie and Coggin,[1] Prinzmetal[2] and Wosnessensky.[3] Total infarction of one kidney may precede that of the other by a considerable length of time.

The diagnosis may be suggested in the course of a detailed history. Associated cardiac disease, with slow or sudden onset of flank or upper abdominal pain, may indicate infarction.

Excretion tests and excretory urograms are, of course, valueless in total bilateral infarction. Retrograde studies in the absence of antecedent renal disease will show a normal pyelogram in the acute phase.[4] Total infarction of long duration produces contracture of the kidney, renal pelvis and calyces. In the presence of acute total infarction, reddish fluid may be obtained on catheterization of the bladder or renal pelvis. This paradoxical finding is not inconsistent but represents hemoglobin laden fluid liberated by autolysis from the infarcted area.[1, 5] Bilateral total infarction accounts for only a small percentage of the anurias resulting from infarction.[1, 6] Most cases of renal infarction dying in anuria show multiple bilateral old and recent small infarcts.

CASE REPORT

The following case report of complete infarction of one kidney, and later exitus from total infarction of the remaining kidney is presented.

Z. F., a 66 year old white woman, was admitted to the Boston City Hospital on the Fourth (Harvard) Medical Service on November 24, 1948. She was apparently well until 5 days prior to admission when she developed nausea and vague abdominal cramps. The next day she resumed her duties as a school teacher. The following day she again experienced moderately severe abdominal cramps, which were more pronounced in the right upper quadrant and associated with nausea and vomiting. She had not voided for some time and consulted her physician, who obtained a small amount of bloody "urine" upon catheterization. Her past history was of interest. She was a known hypertensive for 7 years with mild exertional dyspnea, orthopnea and ankle edema. For 3 years she had been having intermittent claudication. Six months prior to admission, she had one episode of pain, numbness, pallor and coldness of the left lower leg which disappeared spontaneously. She had received digitalis and potassium thiocyanate since the onset of her cardiac symptoms. On examination, the pertinent findings were a blood pressure of 210/90 mm. Hg., cardiac enlargement to the left with an apical systolic murmur. The abdomen was obese with right upper quadrant and right flank tenderness associated with slight spasm. Laboratory studies were noncontributory except for an elevated nonprotein nitrogen of 91 mg. per cent.

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[1] Hoxie, H. J. and Coggin, C. B.: Arch. Int. Med., **65**: 587, 1940.
[2] Prinzmetal, M., Hiatt, N. and Tragerman, L.: J. A. M. A., **118**: 44, 1942.
[3] Wosnessensky, W. P.: Zentralbl. f. Chir., **55**: 651, 1928.
[4] Regan, F. C. and Crabtree, E. G.: J. Urol., **59**: 981, 1948.
[5] Libman, E. and Fishberg, A.: Ann. Int. Med., **11**: 1344, 1938.
[6] Barney, J. and Mintz, E.: J. A. M. A., **100**: 1, 1933.

FIG 1. Retrograde pyelogram Some ptosis and overdistention of right kidney, but otherwise it is within normal limits Left pelvis and its calyces markedly reduced in size. On original x-ray film, left renal outline can be clearly seen to be about one fourth normal size.

Immediately following admission, she was catheterized and only 2 cc red "urine" was obtained. An urological consultation was requested and cystoscopy performed. A few drops of coffee-ground material were found in the bladder. No abnormalities of the bladder were noted. Ureteral catheters were passed to each renal pelvis without difficulty. Two cc of dark reddish fluid were removed from the right kidney and none from the left. Retrograde pyelograms were made (fig. 1).

The patient was placed on constant bladder drainage and was allowed nothing by mouth She received penicillin 100,000 u. prophylactically every 4 hours and a daily intravenous injection of 500 to 1,000 cc 10–20 per cent dextrose in distilled water On her third hospital day she received in addition 700 cc normal saline There was total anuria throughout the entire period. She became progressively drowsy Her nonprotein nitrogen rose to 159 mg. per cent on the seventh hospital day Chlorides ranged from 75–84 meq. CO_2 combining power was re-

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TOTAL INFARCTION OF THE KIDNEYS FROM BILATERAL ARTERIAL EMBOLI

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The anuria accompanying total bilateral renal infarction from arterial emboli may be puzzling to the clinician. It is not the purpose of the authors to indulge in a discussion of the causes and differential diagnosis of anuria, but rather to emphasize an obscure entity of which the urologist should be aware.

Total infarction of the kidneys from bilateral arterial emboli is rare. Hoxie and Coggin[1] in reporting 1 case in 1940 reviewed 14,411 autopsies and failed to find a similar instance of this condition, although 205 of the post-mortem examinations in their large series showed some degree of renal infarction.

Bilateral total infarction does not always occur simultaneously as in the cases reported by Hoxie and Coggin,[1] Prinzmetal[2] and Wosnessensky.[3] Total infarction of one kidney may precede that of the other by a considerable length of time.

The diagnosis may be suggested in the course of a detailed history. Associated cardiac disease, with slow or sudden onset of flank or upper abdominal pain, may indicate infarction.

Excretion tests and excretory urograms are, of course, valueless in total bilateral infarction. Retrograde studies in the absence of antecedent renal disease will show a normal pyelogram in the acute phase.[4] Total infarction of long duration produces contracture of the kidney, renal pelvis and calyces. In the presence of acute total infarction, reddish fluid may be obtained on catheterization of the bladder or renal pelvis. This paradoxical finding is not inconsistent but represents hemoglobin laden fluid liberated by autolysis from the infarcted area.[1, 5] Bilateral total infarction accounts for only a small percentage of the anurias resulting from infarction.[1, 6] Most cases of renal infarction dying in anuria show multiple bilateral old and recent small infarcts.

CASE REPORT

The following case report of complete infarction of one kidney, and later exitus from total infarction of the remaining kidney is presented.

Z. F., a 66 year old white woman, was admitted to the Boston City Hospital on the Fourth (Harvard) Medical Service on November 24, 1948. She was apparently well until 5 days prior to admission when she developed nausea and vague abdominal cramps. The next day she resumed her duties as a school teacher. The following day she again experienced moderately severe abdominal chyma measuring 3.5 by 1.0 by ½ cm. The left renal artery was small and filled with a gray-white thrombus which extended to the lumen of the aorta (fig. 2, *B*).

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[1] Hoxie, H. J. and Coggin, C. B.: Arch. Int. Med., **65:** 587, 1940.

[2] Prinzmetal, M., Hiatt, N. and Tragerman, L.: J. A. M. A., **118:** 44, 1942.

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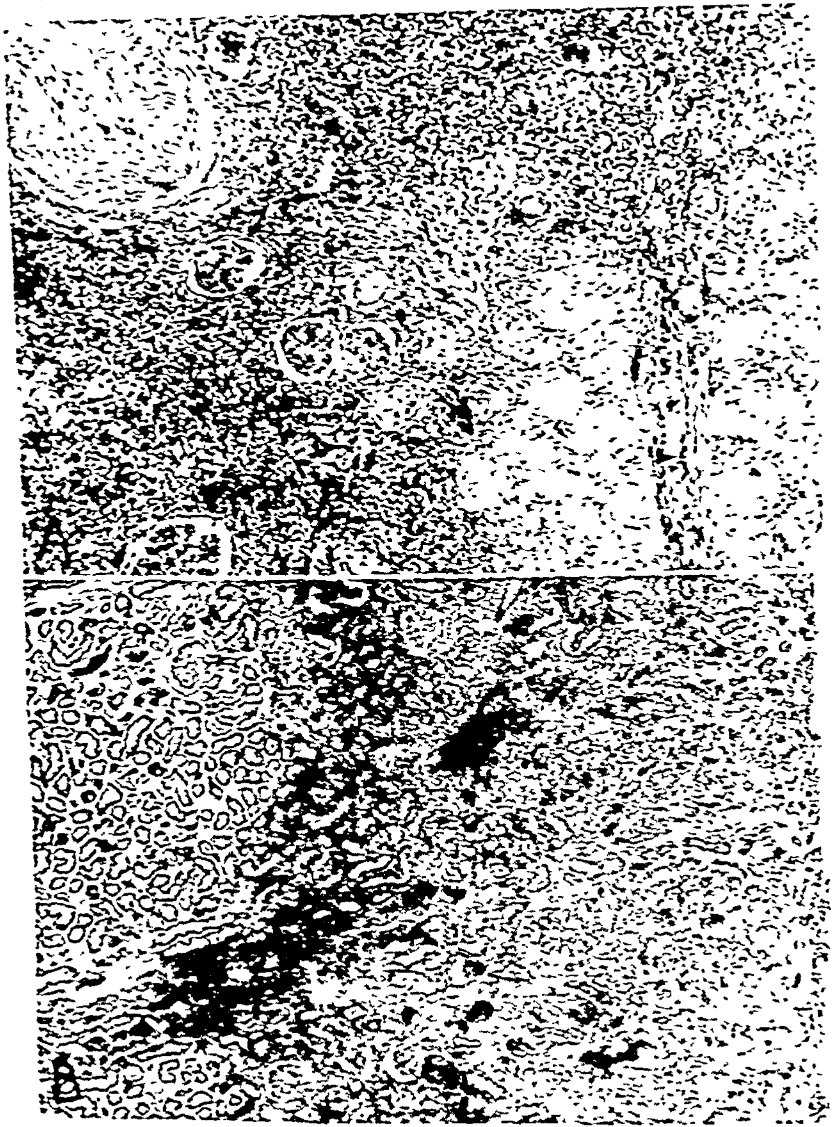

FIG. 3. [illegible] section of shrunken left kidney showing remaining renal tissue adjacent to [illegible]. Arteries [illegible] lower left corner [illegible] small [illegible] *B*, low [illegible] infarcted right kidney showing [illegible] subcapsular [illegible] zone [illegible] of coagulation necrosis.

Microscopic examination showed wide areas of dense collagenous tissue containing ghosts of glomeruli. In the small area of recognizable parenchyma the tissue was compressed, the tubules atrophic, and the interstitial tissue infiltrated ported between 35–42 vol. per cent. An electrocardiogram on the fourth day was considered to be compatible with potassium intoxication. On the ninth day following admission, she was digitalized prophylactically. The same day uncontrolled generalized hyperactivity with muscular twitchings occurred. Carpopedal spasm developed, followed by clonic convulsions and death. The clinical diagnoses were: a) Arterial infarction of the right kidney, b) atrophic pyelonephritic or hypoplastic left kidney, c) arteriosclerotic and hypertensive cardiovascular disease, and d) generalized arteriosclerosis.

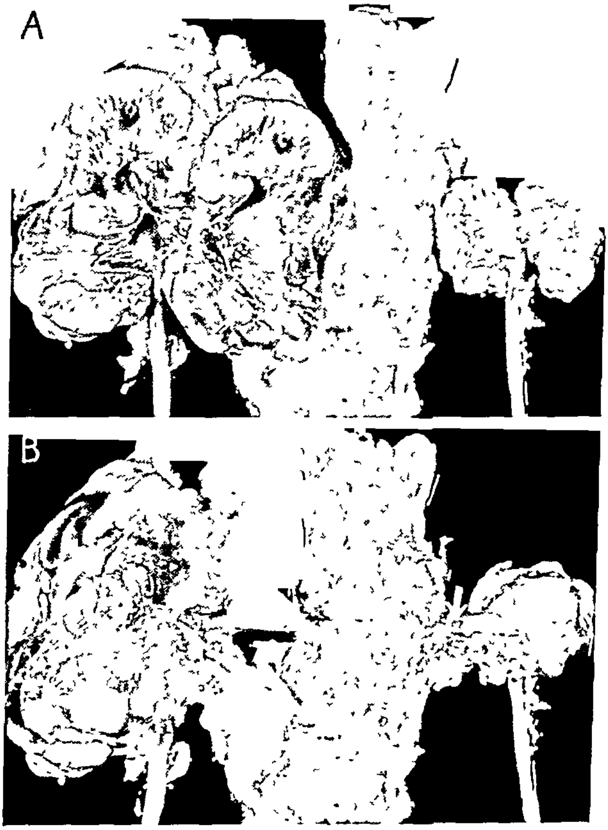

Fig. 2. *A*, large right kidney is infarcted except for small subcapsular zone. Small left kidney largely replaced by fibrous tissue, *B*, right and left renal arteries have been incised longitudinally for short distance near their origin at aorta. Arrows point to old embolus in left renal artery and recent embolus in right renal artery.

Autopsy was performed and the pertinent findings were as follows:

The heart weighed 420 gm. and appeared grossly normal. The myocardial surface showed no areas of scarring or fibrosis. The left auricular appendage revealed an ante-mortem small, red, friable mural thrombus. The coronary system was patent.

The left kidney was recognizable but was largely replaced by fatty and areolar tissue. The organ weighed only 30 gm. (fig. 2, *A*). The cut surface showed almost complete fibrous tissue replacement except for a small portion of renal parenchyma measuring 3.5 by 1.0 by $\frac{1}{2}$ cm. The left renal artery was small and filled with a gray-white thrombus which extended to the lumen of the aorta (fig. 2, *B*).

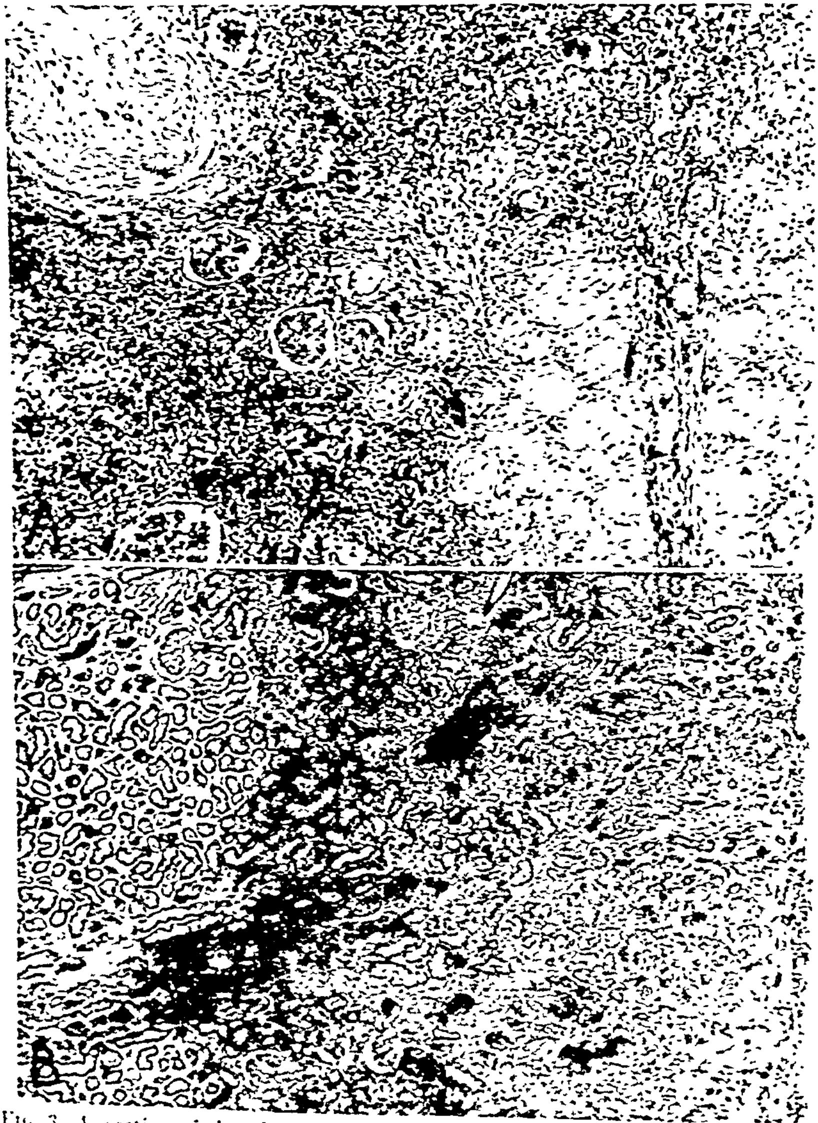

Fig. 3. *A*, section of shrunken left kidney showing remaining renal tissue adjacent to old infarct. Artery at lower left contains some small recanalized vascular channels. *B*, low power view of recently infarcted right kidney showing intact subcapsular zone, hyperemic red zone and third zone of coagulation necrosis.

Microscopic examination showed wide areas of dense collagenous tissue containing "ghosts" of glomeruli. In the small area of recognizable parenchyma the tissue was compressed, the tubules atrophic, and the interstitial tissue infiltrated

ticles obtained the same negative results. Clinically Prinzmetal reported the case of a 53 year old woman with chronic rheumatic heart disease who became hypertensive immediately following total bilateral renal infarction. Bumpus[16] relieved a hypertensive by removing an atrophic pyelonephritic left kidney only to have hypertension recur postoperatively after almost total infarction of the remaining kidney. Foley did not record whether permanent hypertension occurred following the total unilateral infarction in his case. It would seem that if hypertension occurs after total unilateral infarction it is only temporary. Following bilateral total infarction some rise in blood pressure probably occurs and this most likely persists until death.

SUMMARY

Total renal arterial infarction is rare and bilateral total infarction extremely so.

Bilateral total renal arterial embolic infarctions may occur simultaneously or infarction of one kidney may precede that of the other by a considerable period of time.

Unilateral total infarction in a noninfected kidney results in aseptic autonephrectomy. The kidney contracts and on retrograde pyelogram is similar to a chronic atrophic pyelonephritic or hypoplastic kidney.

The pain associated with total infarction is not always severe and is sometimes more abdominal than flank in location.

The anuria associated with total bilateral renal arterial infarction especially in those cases without the typical excrutiating flank pain must be differentiated from anuria due to other causes. An adequate and detailed history is most helpful and associated cardiac disease points to infarction.

If hypertension occurs after total unilateral infarction it is probably temporary. Complete occlusion of both renal arteries may occasion hypertension which persists until death.

333 Linwood Ave., Buffalo 9, N. Y.

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[16] Bumpus, H. C. J. Urol., 52: 295, 1944

with lymphocytes and occasional plasma cells. The arterial system showed thickening of the media and hyalinization of the subintimal area. One small artery was completely thrombosed with apparent recanalization (fig. 3, *A*).

The right kidney appeared larger than normal and weighed 170 gm. The surface was lobulated due to an old infarct. The cut surface was dark red and hemorrhagic with widespread areas of necrosis. Except for a small subcapsular area, the entire organ was involved in the process. A fresh red thrombus projected from the orifice of the renal artery and extended throughout the length of the vessel (fig. 2, *B*). Microscopic examination showed generalized loss of cellular detail and nuclear structure with the exception of a few areas in the subcapsular collecting tubules (fig. 3, *B*).

The final diagnoses were: a) Old complete infarction of the left kidney with subsequent atrophy, b) old right renal infarct, c) recent complete arterial infarction of the right kidney, and d) mural thrombus, left auricle.

DISCUSSION

Experimentally, clamping of the renal artery in dogs for two to three hours has resulted in a walnut sized calcified kidney in about 18 months.[7, 8] Foley[9] was able to follow, clinically, a 55 year old white woman with auricular fibrillation who had sudden left flank pain. An excretory urogram showed an enlarged left kidney with no function and a normal sized and functioning right one. Retrograde pyelograms revealed an essentially negative left pelvis, calyces and ureter. Repeat retrograde pyelograms 2, and 3 months later, showed a marked decrease in the size of the left renal pelvis. Nineteen months later shrinkage had continued to near disappearance of the kidney. Foley's case graphically illustrates that total occlusion of the renal artery of a noninfected kidney results in aseptic total infarction and autonephrectomy. The cycle of the totally infarcted kidney consists of enlargement immediately after occlusion of the artery followed by progressive shrinkage of the entire organ over a period of months resulting in a small functionless kidney. Folsom and Alexander's[10] case of total infarction of the right kidney with unexplained fibrotic atrophy of the left may represent a case similar to ours.

The association of this patient's hypertension to her renal infarction is equivocal. Goldblatt[11, 12] has shown experimentally that unilateral clamping of the main renal artery causes only temporary elevation of the blood pressure for a varying period. Complete occlusion of both renal arteries results in hypertension. Senator[13] injected liquid paraffin into the renal arteries of cats with no resultant rise in blood pressure. Cash[14] found no elevation after injecting insoluble Berlin blue into the renal arteries of dogs. Jensen and Apfelbach[15] using charcoal par-

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[7] Staehler, W.: Beitr. z. klin. Chir., **167:** 189, 1938.
[8] Westerborn, A.: Ztschr. f. Urol., **31:** 687, 1937.
[9] Foley, F. E. B.: Minn. Med., **23:** 136, 1940.
[10] Folsom, A. J. and Alexander, J. C.: Urol. & Cutan. Rev., **38:** 197, 1934.
[11] Goldblatt, H.: Ann. Int. Med., **11:** 69, 1937.
[12] Goldblatt, H., et al.: J. Exper. Med., **59:** 347, 1934.
[13] Quoted by Goldblatt.[11]
[14] Cash, J. R.: Bull. Johns Hopkins Hosp., **35:** 168, 1924.
[15] Quoted by Goldblatt.[11]

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RENAL HAMARTOMA

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Hamartoma has been defined by Albrecht as a tumor due to overdevelopment of some tissue element which belongs normally at the site where it is found, or to an abnormal relationship of a normally situated tissue element. These tumors are rare, and, because of the varied gross and microscopic pattern which they may present, they are often diagnosed incorrectly. They are essentially benign, but areas of the tumor, either malignant or potentially so, have been described.

In the urinary tract hamartoma has been found mainly in the kidney cortex. Davis described one of the urinary bladder, and in the case records of the Massachusetts General Hospital is described a hamartoma of the renal pelvis, which was thought to have arisen from cloacal remnants.

Hamartoma of the renal cortex may occur clinically as an isolated entity or as part of the syndrome described by Moolten as the tuberous sclerosis complex. Moolten states that the lesions of this syndrome represent "a widespread developmental anomaly, often hereditary, in which the primary abnormality lies in the faulty differentiation of tissues rather than of body units (although the latter may be included). The individual lesions present the characteristics of hamartia or of hamartomas, regardless of their situation." Jacobaeus, as early as 1903, and Vogt, in 1908, emphasized also that the brain, skin, and visceral changes of tuberous sclerosis were similar in nature and constituted but different lesions of an identical disease.

A brief summary of the lesions of the tuberous sclerosis complex is as follows:

1) The brain lesions have been designated as tuberous sclerosis. This is a rare disease first described by Bourneville and Brissand in 1880. Approximately 130 cases, diagnosed pre-mortem, have been reported to date.

Typically there are sclerotic nodules throughout the brain, containing glial cells, and about which there is disorientation and atrophy of the nerve cells. In time, calcium may be deposited in these nodules and may be demonstrable during life by x-ray examination. These nodules may become glioblastic.

Clinically, there is mental and often physical retardation, appearing usually in infancy or early childhood. As life progresses mental deterioration progresses, and institutionalization is often required. Very common are epileptiform seizures or their equivalents, which vary in type, frequency, and duration. These may begin early in infancy, or the onset may be about the time of puberty. Early in infancy the only mental aberration may be nervous attacks of screaming, crying, etc. Nearly all affected with tuberous sclerosis die in childhood or early adulthood, most commonly of status epilepticus, infection, or cachexia.

2) The most common skin lesion of the tuberous sclerosis complex is adenoma

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sebaceum This lesion is almost always present It consists of small, greasy, grey-red papules distributed in butterfly fashion across the bridge of the nose, over the cheeks and chin, and especially in the nasolabial folds These usually appear during childhood, and they persist more or less unchanged for life They are asymptomatic, being only of cosmetic importance to the patient

Many other skin lesions have been described, such as subungual and peri-ungual fibromata collagenous plaques, cutaneous polypi, intradermal nodules, and Shagreen patches Gingival and lingual tumors may be seen There may be changes in pigmentation, as vitiligo and café au lait

3) Visceral tumors may occur at widespread sites Perhaps the most common is phacoma of the retina, which appears as white or grayish and irregularly rounded usually multiple, areas These rarely grow in size, but they may become calcified or cystic, and they may cause visual disturbances It has been said that they are a duplication of the process which is developing in the brain

Hamartoma of the heart, often described as rhabdomyoma, may give clinical evidence of cardiac disease Visceral tumors have also been described in the liver, spleen, bone, kidney, and other organs

Of greatest interest to the urologist is the renal tumor These are present, according to Critchley, in 80 per cent of cases of tuberous sclerosis They are rarely diagnosed during life, but are found usually at autopsy, probably because they are quite benign and asymptomatic and because patients with tuberous sclerosis complex usually die early in life They are often multiple and bilateral, and that they may occur early is demonstrated in the case of Piatt-Thomas who found, at autopsy, tumors both of the kidneys and heart of a premature infant. These tumors may attain large proportions, and, if bilateral, multiple, and large, they may cause renal insufficiency We can find but 5 reported cases of renal tumor associated with tuberous sclerosis complex, diagnosed during life, in the American literature We find references to 12 more such cases, diagnosed during life, in the foreign literature

In the reported cases of the renal tumors associated with the tuberous sclerosis complex many diagnoses as to the type of renal tumor have been made Vogt, Froug Fischer, Harbitz, and Fish and McLaughlin designated the tumors in their cases as liposarcoma, Hyman de Montet, Marcuse, and Bonfigli described hypernephromas, Campbell, an endothelioma, Gavazzeni, an angiofibroma; Critchley and Earl, a perithelioma and mixed sarcoma Moolten and Mertz indicate that at least some of these growths belong rightfully with the renal nodules of the tuberous sclerosis complex It seems likely that the entity represents a dysplastic rather than a neoplastic lesion

For more detailed discussion of the various lesions of the tuberous sclerosis complex, reference is made to the excellent treatises of Moolten, Mertz, Fischer, and others With this brief review of the syndrome, we wish to report a typical case with renal hamartoma—the sixth diagnosed during life and reported in the American literature—and also a case of renal hamartoma occurring without other evidence of the tuberous sclerosis complex, a case type which is mentioned but which we have not found reported in the American literature

CASE REPORTS

Case 1. Miss T. E., a 42 year-old white woman, was first seen on February 24, 1949. Twelve days previously, while preparing a meal, she felt nauseated and others present had told her that she looked pale. She became faint and felt pain in the right flank, which lasted for 4 or 5 days. Her referring doctor told her that she had a kidney tumor. She had no other urological symptom.

On examination, there was an 8 by 4 inch mass palpable in the right flank, which moved with respiration, and which felt firm and slightly irregular. It was not tender. Cystoscopy and retrograde pyelography revealed a large, rounded, lower pole enlargement of the right kidney, deforming the calyces (fig. 1). She was admitted to St. John's Hospital, Tulsa, on February 28, 1949, with a diagnosis of right renal tumor.

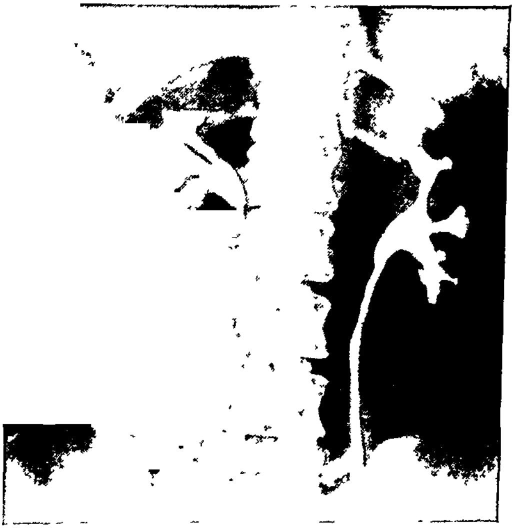


Fig. 1

According to the relatives, this patient had always been somewhat retarded mentally, and her growth and development were slow. In early infancy she was known to have had a few convulsive seizures. At about the age of 16, she began to have seizures typical of epilepsy, and these subsequently occurred once or twice just before and just after each menstrual period. In 1946 dilantin was prescribed, and she has had no attacks since. With these attacks, there was no aura, and she would fall only at times. Loss of bladder control and biting of the tongue had been noted.

The patient also had had a rash across the bridge of the nose, extending onto the cheek, and into the nasolabial folds as long as she could remember. Since about age 18, she had had small growths appearing about the margins of the toenails on both feet.

The father of this patient had a nephrectomy for renal tumor in 1929, and 6 months later lymph glands were removed from the groin. The pathologic diagnosis of the tumor in the kidney and in the lymph glands was hypernephroma. This diagnosis, according to the hospital records, was made from frozen sections, and the slides could not be found for review. The father died 17 years after that operation of an acute cardiac condition. He was in good health until the day of his death. He had lesions of the face, the same as the patient for as far back as the relatives can remember, but they had noticed no mental disorder, eye difficulty, or other stigmata suggestive of the tuberous sclerosis complex. The mother is at present in a mental institution, but has no lesions as are present in the patient or her father. The patient has no siblings.

Examination revealed a large, well nourished, cooperative white woman, weighing 225 pounds. On the face was a symmetric telangiectatic papular lesion, chiefly over the malar area, across the bridge of the nose and across the cheeks. The lesions were most prominent and characteristic in the nasolabial folds (fig. 2, A). In the right flank, extending into the right upper quadrant there was a firm, irregular mass, moving with respiration, and nontender. From under the distal edge of the toenails of the first, second, and third toes of each foot, arose rather firm, purplish, fleshy tumors, which were nontender, and which measured up to 0.5 cm. in diameter. The nails were markedly cornified (fig. 2, *B*).

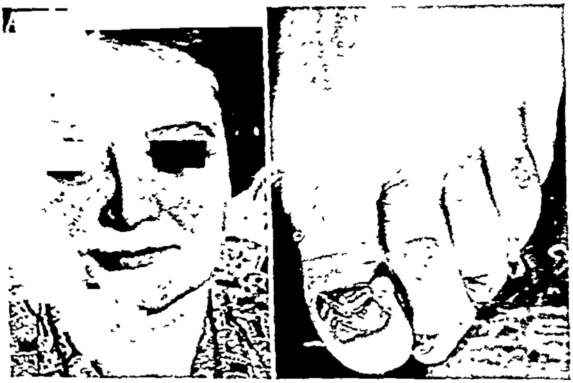


FIG. 2

Hemoglobin was 10.9 gm. per cent. Erythrocytes numbered 3,530,000 and leukocytes numbered 5,100 per cubic millimeter of blood. The differential blood count was normal.

Radiograms of the skull revealed scattered calcifications throughout the cortex, which were typical of tuberous sclerosis (fig. 3). The electrocardiogram was normal. Wechsler Bellevue IQ was 68 on two occasions. Electro-encephalography revealed predominantly 9–11 sec. activity in all leads. There were many runs of 15–20/sec. in all leads. There was little build up with hyperventilation. Radiogram of the chest was normal, as was an x-ray study of the bones of the hands. Ophthalmoscopic examination revealed no evidence of phacoma.

The small tumors about the toenails were biopsied and microscopically were found to consist of pieces of skin covered by hyperkeratotic stratified squamous epithelium. The cuticular and subcuticular tissues were occupied by an admixture of numerous tiny capillaries and foci of adipose tissue and intertwining fasciculi of fibrous connective tissues and smooth muscle, typical of hamartoma of the skin.

FIG. 3

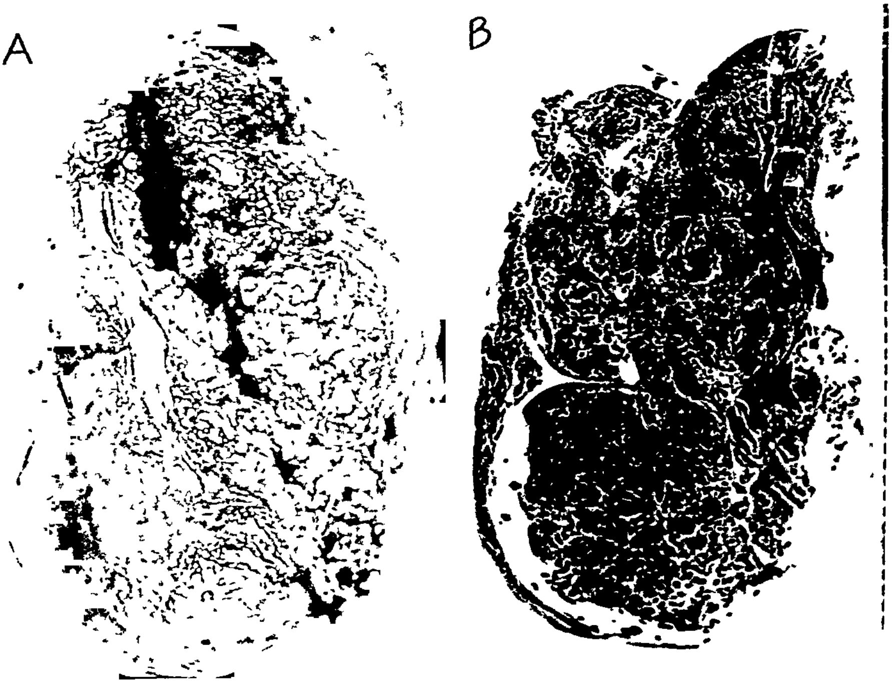


FIG. 4. *A*, kidney, right, with multiple small hamartomas, second large hamartoma, left, attached to kidney. *B*, longitudinal section through kidney and attached large segment of tumor Note multiplicity of hamartomas within renal cortex Large segment of tumor to left was attached to kidney by only small bridge of hamartomatous tissue

The patient was given transfusions of whole blood and other preoperative preparation. On March 1, 1949, right nephrectomy was carried out by the lumbar approach. A large tumor of the lower pole was found, and the kidney and tumor were removed en toto (fig. 4).

The pathologic specimen consisted of a kidney and surrounding perirenal tissues measuring 10 by 10 by 16 cm. The capsule of the kidney was stripped away with difficulty, revealing a finely granular kidney surface which contained numerous soft yellow masses measuring up to 1.5 cm. which were scattered over the entire surface. At the lower pole of the kidney one of these masses extended into the surrounding perirenal tissue and connected with a soft yellow necrotic mass measuring 10 cm. in the greatest diameter. Along one border of this there was a hematoma measuring 5 cm. in greatest diameter. The cortex of the kidney measured 0.6 cm. in thickness and was not clearly demarcated from the medulla. No gross abnormalities were noted in the calyces and pelvis. Microscopically (fig. 5) there were numerous dysplastic formations scattered throughout the medulla, cortex, and portions of the perirenal tissues. These were composed in some areas of normal adipose tissue and in other areas of interlacing fasciculi composed of normal fibrous tissue. The several elements were intermingled with one another in various proportions. In some areas there was a concentration of medium sized arteries, from some of which connective tissue radiated in perithelioid fashion. No bizarre mitoses were present. Diagnosis: hamartoma of the kidney.

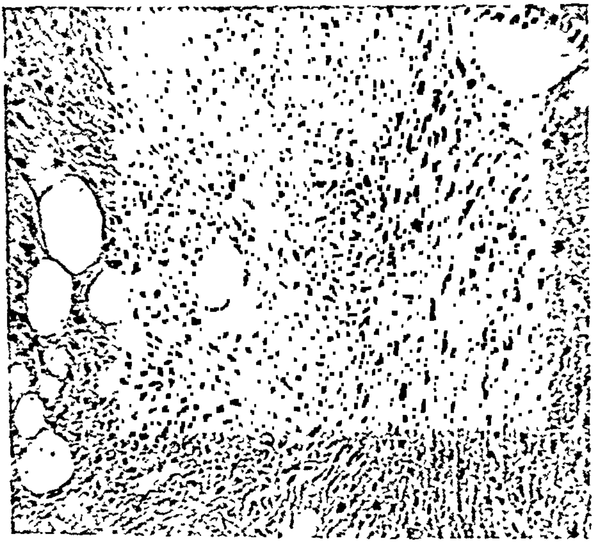


FIG. 5

The postoperative course was essentially uneventful, and the patient was discharged from the hospital on the twelfth postoperative day.

The patient has continued to be in good condition, with no evidence of recurrence of tumor. Her seizures remained under control with dilantin.

Case 2. Miss M. M., 59-year-old white woman, was admitted to St. John's Hospital. Tulsa, on April 24, 1950. Three days prior to admission she had had a chill, and since had noted an irregular fever to 103F. She had had slight bladder irritation but no other symptoms. Upon finding her urine to be loaded with fasciculi of fibrous connective tissues and smooth muscle, typical of hamartoma of the skin.

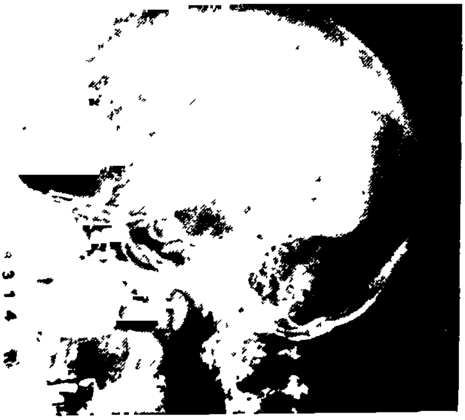
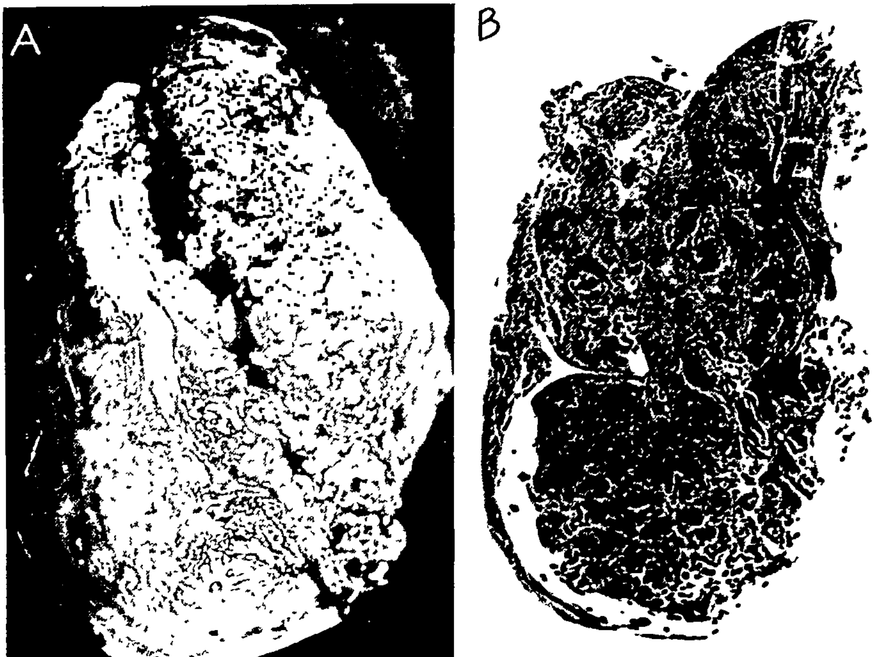


FIG. 3



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The patient was given transfusions of whole blood and other preoperative preparation. On March 1, 1949, right nephrectomy was carried out by the lumbar approach. A large tumor of the lower pole was found, and the kidney and tumor were removed en toto (fig. 4).

The pathologic specimen consisted of a kidney and surrounding perirenal tissues measuring 10 by 10 by 16 cm. The capsule of the kidney was stripped away with difficulty, revealing a finely granular kidney surface which contained numerous soft yellow masses measuring up to 1.5 cm. which were scattered over the entire surface. At the lower pole of the kidney one of these masses extended into the surrounding perirenal tissue and connected with a soft yellow necrotic mass measuring 10 cm. in the greatest diameter. Along one border of this there was a hematoma measuring 5 cm. in greatest diameter. The cortex of the kidney measured 0.6 cm. in thickness and was not clearly demarcated from the medulla. No gross abnormalities were noted in the calyces and pelvis. Microscopically (fig. 5) there were numerous dysplastic formations scattered throughout the medulla, cortex, and portions of the perirenal tissues. These were composed in some areas of normal adipose tissue and in other areas of interlacing fasciculi composed of normal fibrous tissue. The several elements were intermingled with one another in various proportions. In some areas there was a concentration of medium sized arteries, from some of which connective tissue radiated in perithelioid fashion. No bizarre mitoses were present. Diagnosis: hamartoma of the kidney.

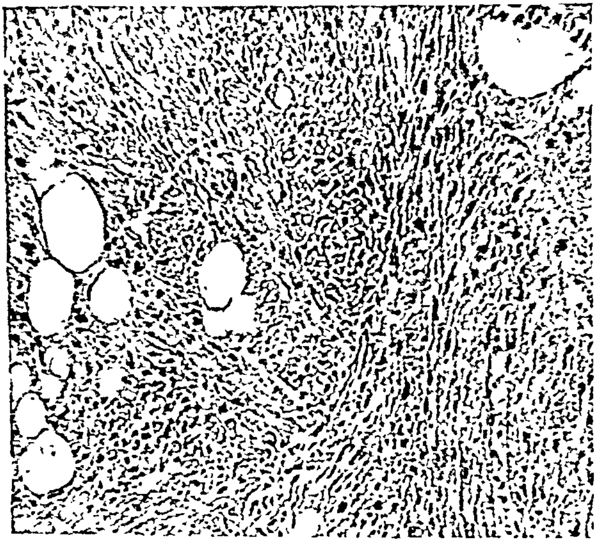

Fig. 5

The postoperative course was essentially uneventful, and the patient was discharged from the hospital on the twelfth postoperative day.

The patient has continued to be in good condition, with no evidence of recurrence of tumor. Her seizures remained under control with dilantin.

Case 2. Miss M. M., 59-year-old white woman, was admitted to St. John's Hospital, Tulsa, on April 24, 1950. Three days prior to admission she had had a chill, and since had noted an irregular fever to 103F. She had had slight bladder irritation but no other symptoms. Upon finding her urine to be loaded with pus cells she was admitted to the hospital for treatment of a urinary tract infection.

Past history revealed that for several years she had taken thyroid in small doses due to a reputedly low basal metabolic rate. She had had tuberculosis of the left eye in 1940. For the past several years the process had apparently been quiescent.

Physical examination revealed an obese woman who weighed 304 pounds. The blood pressure was 116/70, and there was an umbilical hernia of small proportions. There were moderate varicosities of the right lower extremity, but otherwise general physical examination was not remarkable.

The urine was loaded with leukocytes, but was otherwise normal. Routine blood studies were within normal limits.

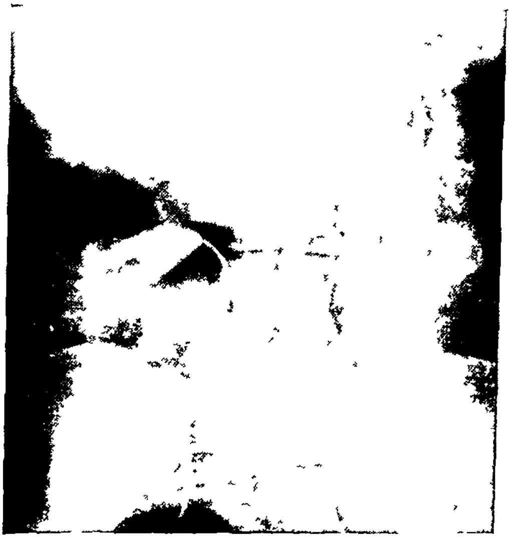

FIG. 6

With chloromycetin in therapeutic dosage the temperature subsided to normal within 72 hours, and the urine became normal. In the course of routine urologic study, to determine any cause for the urinary tract infection, retrograde pyelograms were carried out, and these revealed a deformed right renal pelvis which was displaced downward (fig. 6). The nature of the cause of the deformity could not be determined, since, due to the marked obesity of the patient, no x-ray studies could be considered adequate. However, gastro-intestinal series, gallbladder series, barium enema studies, and chest and skull radiograms all appeared to be normal. Exploratory operation was advised and carried out on May 13, 1950. At operation a tumor about two inches in diameter was found bulging from the surface of the kidney along the lateral border, in the upper one-third of the kidney. The tumor and kidney were removed en toto.

The postoperative course was entirely uneventful, and the patient left the hospital on the fourteenth postoperative day. Electrocardiogram and ophthalmoscopic examinations have been carried out and are normal. The Standard-Binet Test revealed an IQ of 146.

The pathological report of the surgical specimen was as follows:

The pathologic specimen consisted of a kidney measuring 10 by 7 by 5 cm., weighing 170 gm. A 3 cm., mottled gray and white, rubbery, irregular nodule protruded above the renal surface, along its lateral aspect, in the midportion of the kidney. On section, the nodule extended into the kidney, through the cortex, to a depth of 1.5 cm. and was sharply delimited from it. Its cut surfaces were mottled yellow and gray. A similar, 0.5 cm. nodule was present within the renal cortex, 2 cm. distal to the larger lesion. The remainder of the kidney, calyces, pelvis, and ureter were grossly normal. Histologic examination "reveals a dysplastic conglomeration of tissues (fig. 7) consisting of varying proportions of adipose tissue, blood vessels, fibrous tissue, and smooth muscle. The fibroblastic tissue in some areas is loosely knit and mesenchymal in type, being composed of spindle shaped cells having small to moderately large, oval, hyperchromatic nuclei. In some areas this tissue is more compact with formation of intertwining fasciculi of fibrous tissue and smooth muscle. Capillaries and bizarre arterioles incorporated within the mesenchymal tissues form a prominent feature of the lesion in some areas. The arterioles in some areas are partially devoid of media and are composed of loosely knit fibroblastic tissue which becomes dispersed out into the surrounding stromal elements in a concentric fashion. No epithelial elements are demonstrable within the lesion. Several similar small dysplastic foci are scattered throughout other portions of the cortex and medulla of the kidney. The renal tissue immediately adjacent to these lesions presents hyalinized, obliterated glomeruli and arterioles and atrophic tubules within a narrow

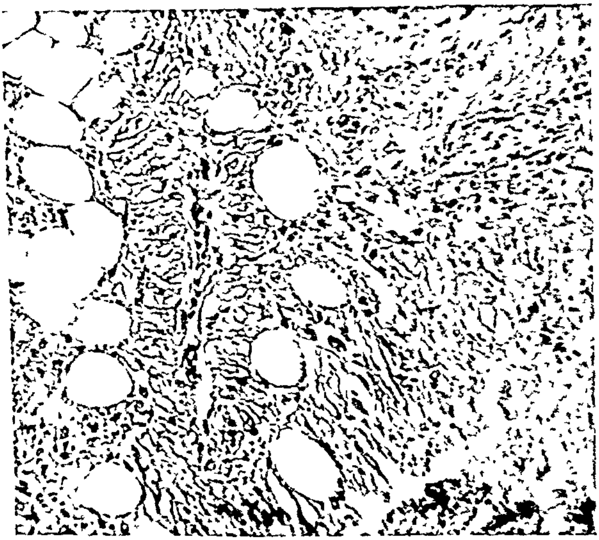

FIG. 7

zone which is infiltrated by numerous lymphocytes. The intervening renal parenchyma exhibits no abnormalities in the glomeruli, arterioles, tubules, or submucosa of the calyces and pelvis."

COMMENT

Case 1 is a typical case of tuberous sclerosis complex as described by Moolten. The brain lesions of tuberous sclerosis, hamartomas of the skin and kidney, mental deterioration and epilepsy have been illustrated. Also noted in this case is a family history of the condition, which is very important. We believe that we are correct in assuming that the father of this patient had tuberous sclerosis complex with adenoma sebaceum and renal tumor. The diagnosis of hypernephroma was probably incorrect, since no detailed description of the sections was made and it would be unusual for an individual with a hypernephroma with metastasis to live 17 years without evidence of recurrence of tumor.

This case is particularly interesting because of the age of the patient, and because of the fact that she has gone 42 years without having more severe, and perhaps fatal, neurologic manifestations. Having had a benign tumor, and because her mental retardation is not marked and her epilepsy is, at the present time, well controlled, her prognosis is still undoubtedly better than the average with this disease. It will be interesting to see what her status is after she passes through the menopause, since the stigmata of tuberous sclerosis complex may appear, or, in other cases, become more pronounced, at adolescence.

Case 2 is of a hamartoma of the kidney occurring as a separate entity. Other stigmata of the tuberous sclerosis complex were not evident in this case. It is interesting, but probably coincidental, that both patients were very large and obese. Examination of the microscopic sections of the tumors in these cases proves them to be practically identical, both being typical hamartomas. The prognosis in this case as regards the renal lesion, as in the other case, is good.

Neither of these patients were given x-ray therapy since, according to Mertz, it has very little effect on these benign tumors.

CONCLUSIONS

A case of tuberous sclerosis complex with renal hamartoma is reviewed, the sixth such case diagnosed during life to be found in the American literature.

A case of renal hamartoma, occurring apparently as an isolated pathological entity, and unlike any case that we have found in the American literature, has been described.

A brief description and review of the literature of the tuberous sclerosis complex and the relation of renal hamartoma to this syndrome, has been presented.

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REFERENCES

ALBRECHT, E.: Verhandl. d. deutsch. path. Gesselsch., 7: 153, 1904.
BONFIGLI, R.: Quoted by Mertz.
BOURNEVILLE: Arch. de Neur., 1: 81, 1880-81.

Campbell, A. W.: Brain, **28:** 367, 1905.
Case Records of the Mass. Gen. Hosp., New England J. Med., **240:** 891, 1949.
Critchley, M. and Earl, C. J. C.: Brain, **55:** 311, 1932.
Davis, T. A.: Northwest Med., **48:** 182, 1949.
De Montet, C.: L'Encephale III, p. 97, 1908.
Fischer, W.: Ziegler Beitr. z. path. anat. u. z. allg. Path., **50:** 235, 1911.
Fish, G. W. and McLaughlin, W. L.: J. Urol., **55:** 28, 1946.
Froug, C.: J. Urol., **45:** 290, 1941.
Gavazzeni, J.: Quoted by Mertz.
Harbitz: Centralbl. f. allg. Path. u. path. Anat., **23:** 868, 1912.
Hyman, A.: J. Urol., **8:** 317, 1922.
Jacobaeus: Nordisk mediciniskt Arch. Stockholm, **36:** 1, 1903.
Marcuse, H.: Neural. Zentralbl., p. 124, 1909.
Mertz, H. O.: Trans. Am. Assoc. Genito-Urin. Surg., **35:** 73, 1942.
Moolten, S. E.: Arch. Int. Med., **69:** 589, 1942.
Pratt-Thomas, H. R.: Am. J. Path., **23:** 189, 1947.
Vogt: Munch. med. Wchnschr., **57:** 2037, 1908.

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THROMBIN IN TREATMENT OF HEMATURIA OF RENAL ORIGIN

ERNEST O. NAY AND ROBERT R. BROWN

The purpose of this brief report is to describe a method which we have found to be of use in the conservative management of renal hematuria. This method has not been properly evaluated because we have not had enough suitable cases, but it seems rational, harmless, and worthy of further trial.

The preparation used was thrombin, an extract of bovine plasma. It has long been used in urology, particularly in prostatic surgery, but its use in the control of renal bleeding has not been reported, at least according to our review of the literature. This hemostatic extract is supplied in powder for topical application as well as in liquid form.

Reports show that many kidneys have been removed as a life-saving measure because of uncontrollable bleeding from a nonsurgical lesion, such as so-called essential hematuria, nephritis, blood dyscrasias, etc. Many drugs, vitamins, venoms, etc. have been used, but with very little success. Dr. Hugh Young (*Young's Practice of Urology*, p. 261) states that the treatment which has given him the best results in such cases is as follows: administration of horse serum intravenously, blood transfusions, and the most important of all, intrapelvic lavages, using 2 to 3 cc of 1:1000 adrenalin or a like amount of 1 per cent silver nitrate, slowly instilled through a ureteral catheter into the pelvis of the kidney. Since the instillation of such solutions seemed to be of benefit, it seemed logical to assume that the bleeding might be from a local lesion in the kidney pelvis or calyces and would, therefore, be accessible to a solution of thrombin. Accordingly, we have tried this method in 3 cases and the following brief report is presented.

O. F., a 62 year old white man, was first seen in 1941, complaining of painless hematuria of 2 weeks' duration and with the history of such episodes of hematuria for 10 years. In 1931, he had required 7 cystoscopic procedures before the bleeding, which was said to have been of right renal origin, was controlled. Similar episodes had occurred at intervals of 2 to 6 months, the bleeding subsiding spontaneously or with oral medication. The history was otherwise negative, as were the physical examination and laboratory studies, and the only positive finding was blood seen coming from the left ureteral orifice. Bilateral retrograde pyelograms were considered to be within the limits of normal. The treatment consisted of intrapelvic lavages, using 2 to 3 cc of 1:1000 adrenalin, vitamins, ferrous sulfate, etc., and he gradually improved.

He was next seen in December 1948, stating that he had continued to pass bloody urine at irregular intervals in the interim, but that the bleeding had been profuse for the last 2 weeks. Studies included a complete history and physical examination, complete blood count, bone marrow biopsy, urinalysis, guinea pig inoculation of urine, urine culture, blood chemistry, serology, cystoscopy and retrograde urograms. All of the findings were within normal limits and the only lesion found was the left renal hematuria. The diagnosis was essential hematuria.

Read at annual meeting, North Central Section, American Urological Association, Grand Rapids, Mich., October 8, 1949.

A pelvic lavage using adrenalin was done following pyelography; however, he continued to bleed, and returned in January with a hemoglobin of only 8.6 gm. and 3,570,000 red cells. Again a pelvic lavage was performed but without benefit. He was hospitalized and three 500 cc blood transfusions given. Still he bled. A ureteral catheter was anchored to the left kidney, but for several days the urine continued to be grossly bloody. On February 15, 1949. 5000 units of thrombin in 5 cc of diluent were instilled into the kidney through the indwelling ureteral catheter. The catheter which had previously drained well apparently became obstructed by clots as it would no longer irrigate following this instillation, and it was removed. For the next 2 days the patient passed clots, but the urine was noticeably clearer. He complained of renal colic for the first time, apparently due to the passage of the clots. His urine became grossly clear on February 18, three days after instilling thrombin, and remained so until his discharge, 1 week later. He was next seen in the office on April 14, seven weeks later, with a relatively slight hematuria of a few hours' duration, the first since instilling thrombin. By the next day the bleeding had subsided. The blood study in April showed 14.5 gm. hemoglobin, with 4,800,000 red cells. A recent contact revealed that there has been no hematuria since then.

We have had 2 other cases in which this method was used, both with good results but without having tried the older measures first, one polycystic disease, the other, essential hematuria.

We have no intention of trying to draw any conclusions from 3 cases, but believe that the method is worthy of a trial. The only possible danger would seem to be inadvertent intravenous injection with intravascular clotting and thrombosis, but this possibility seems remote.

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ATTAINMENT OF EQUILIBRIUM BETWEEN PLASMA AND URINE, WITH REFERENCE TO MEASUREMENT OF RENAL CLEARANCES

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Despite simultaneous intravenous injections p-aminohippurate (PAH)* appears in the urine 2–4 minutes before phenolsulfonphthalein (PSP). This difference in rate of appearance initiated a study of the time necessary to attain constant urinary excretion of a substance (UV) under a steady plasma concentration (P).

METHODS

A rapid (0.5 minute) initial, and a simultaneous slow intravenous infusion of PAH, PSP and mannitol (M)[1] or thiosulfate (TS)[2] were begun. Immediately following this initial injection urine was collected by ureteral catheter for short periods. A Bayliss pump maintained the slow intravenous infusion at a constant rate. Under such conditions a relatively stable plasma concentration of each substance was attained fairly rapidly, leading ultimately to a constant rate of excretion (UV) and to a constant clearance (UV/P). The assumptions are made a) that throughout the observation the renal plasma flow and filtration rate are constant and b) that the attainment of a steady clearance value denotes that kinetic equilibrium between blood and ureteral urine has been reached.

The patients had unilateral kidney disease (pyelonephritis, hydronephrosis, or nephrolithiasis). The opposite kidney was considered normal a) if it had never produced renal symptoms, b) if the clearance values fell within the normal range, and c) if the urine at the time of ureteral catheterization was sterile. With the exception of table 1 only normal kidneys are reported here.

The fasting patient drank a liter of water at 10 p.m. the night before and another liter at 7 a.m. on the day of the test. Between 8:30 and 9:00 a.m. an 8F multi-eyed whistle tipped ureteral catheter* was inserted 15 cm. into each ureter.[3] After withdrawal of the cystoscope an 18F multi-eyed latex urethral

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This work was done while the senior author was a National Research Council fellow in the Medical Sciences.

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We are indebted to Dr. Howard Jeck and Dr. Robert Hotchkiss for their kind cooperation and generosity in allowing us to study patients from the Urology Section of the Second Surgical Division (Cornell) of Bellevue Hospital.

Note by editor. This paper was one of the essays that was awarded a prize in 1948 by the Committee on Scientific Research, American Urological Association, Dr. Miley B. Wesson, chairman.

* We are indebted to the Medical Research Division of Sharp and Dohme, Inc. for an adequate supply of p-aminohippuric acid and mannitol, the latter being used in place of thiosulfate in a few cases.

[1] Smith, W. W., Finkelstein, N., and Smith, H. W.: J. Biol. Chem., **135:** 231, 1940.

[2] Newman, E. V., Gilman, A. and Philips, F. S.: Bull. Johns Hopkins Hosp., *79:* 229, 1946.

* The multi-eyed ureteral catheters have 6 eyes distributed over the proximal 5 cm.

[3] Chasis, H. and Redish, J.: Arch. Int. Med., **70:** 738, 1942.

catheter was inserted into the bladder. During the course of the clearance measurement, the bladder was washed frequently to measure any urinary leak around the ureteral catheters. The clearance determinations on the bladder urines were less than 10 and usually less than 5 per cent of the clearance values of the good kidney. A blank urine (U_0V) was usually collected to determine the rate of excretion of endogenous material reacting in the mannitol or thiosulfate methods. The priming injection and constant infusion were started just as the blank U_0V was terminated. Urine collection during the following 40 minutes was separated into intervals such that the urine output from the kidney with the smaller flow should exceed 2 cc. In this rapid sequence of collections the shortest urine period was 3 minutes and the longest 8. Following this 40 minute period 3 ten minute periods were collected. The average of the last 3 periods was taken as the equilibrium clearance value. During this 30 minute period the transport of all test substances from blood to pelvic urine had reached a steady excretory state.

A blood sample for blank analysis was obtained from an indwelling needle in an antecubital vein before or during the cystoscopic examination. Samples taken at frequent intervals after the priming injection served to define the plasma concentrations of the test substances during the period of rapid change. The priming dose of the test substances was calculated to produce the desired concentration in the estimated extracellular fluid. Since the rates of renal excretion were known from previous clearances on the same patient it was possible to adjust the infusion rate to equal renal excretion, enabling the plasma concentration to become constant as speedily as possible. Clearances were calculated using the plasma concentration at 2.5 minutes before the midpoint of each urine collection period.

RESULTS

Figure 1 shows the average clearance values at 10 minute intervals distributed throughout a 70 minute period as interpolated from 150 clearance periods on 7 normal kidneys. These values are expressed in percentile terms relative to the ultimate clearance values attained after 40 minutes. Similarly, the average plasma concentrations of PAH, TS and PSP interpolated from 93 observations are shown at the same 10 minute intervals in percentile terms relative to the values attained after 40 minutes.

Shortly after the priming injection and while the plasma concentrations of all substances are falling the renal clearances of PAH and TS increase and reach clearance equilibrium after 20 minutes, while PSP does not become stabilized until 30 minutes. That this phenomenon is attributable to a physical factor (washing out the renal dead space) is shown by the fact that this delay time is independent of a rising (fig. 2, *A*) or falling (fig. 2, *B*) plasma concentration. In all instances, the clearances start from low values at 0 time and reach a maximal steady level after 20 minutes. Figure 1 also reveals that the 3 test substances attain equilibrium clearance values at different rates in the order of PAH, TS and PSP. This has been repeatedly observed in the normal and diseased kidney and possible reasons for it are discussed below.

Brun, Hilden and Raaschou,[4] in criticizing the single injection clearance method, show that if the blood concentration of a substance excreted by the kidneys is falling the arterial plasma concentration is always less than the simultaneous venous plasma concentration. Since, in our earlier observations, we used blood from the antecubital veins 2 additional experiments were performed, drawing blood from an indwelling femoral arterial needle. In figure 3, *A* ureteral catheters were inserted 20 cm. into each ureter using the same technique as described above. As the insertion of ureteral catheters can cause temporary reflex oliguria or anuria which might prolong the time to reach clearance equilibrium, an additional experiment (fig. 3, *B*) was performed using an indwelling femoral arterial needle and a soft multi-eyed latex rubber urethral catheter. Since the arterial concentration is less than the venous concentration, the use of arterial blood raises the clearance during the period when the plasma concentration is decreasing. Neither the choice of arterial blood nor the insertion of ureteral catheters has any effect, however, on the delay in attaining clearance equilibrium.* In these experiments the excretion of PAH was appreciably ahead of the excretion of TS.

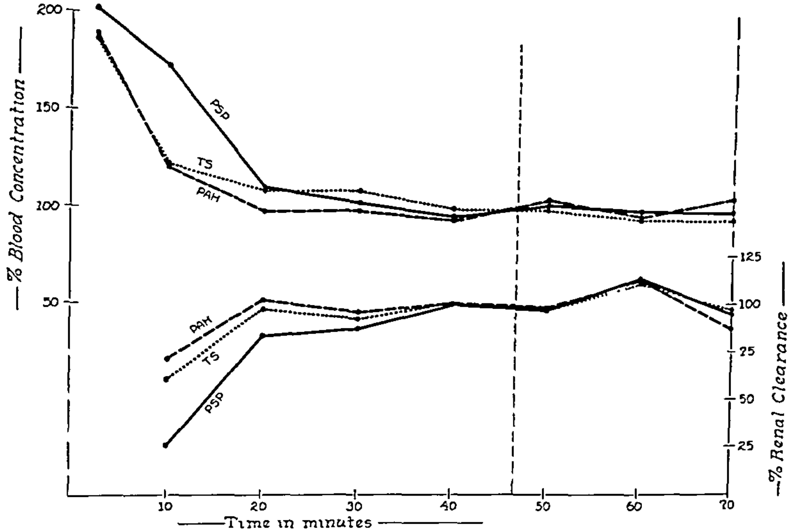

FIG. 1. Rate of attainment of equilibrium clearances (lower curves) in 7 normal human kidneys, in relation to plasma concentrations (upper curves). All data are expressed in percentile terms relative to average of observations, beyond dotted line, made after 40 minutes (equal 100 per cent). Observed data from 5 to 15 minutes, 15 to 25 minutes, etc., were averaged and mean point plotted at 10 minutes, 20 minutes, etc. While plasma concentration of test substances is decreasing, it takes 20 minutes for stable clearance equilibrium.

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[4] Brun, C., Hilden, T. and Raaschou, F.: J. Clin. Investigation, **28:** 144, 1949.

* The high clearance values obtained prior to equilibrium reflects the difficulty in selecting the blood concentration which forms a particular sample of urine. If we adopt Brun's method and select the plasma concentration 7 to 8 minutes before the midpoint of the urine collection period, the plasma concentrations for the first clearance period in figure 3, *A* and *B* are zero and the clearances are infinite!

Similar observations have been made on pyelonephritic kidneys where differential disturbances of glomerular and tubular function might be anticipated.

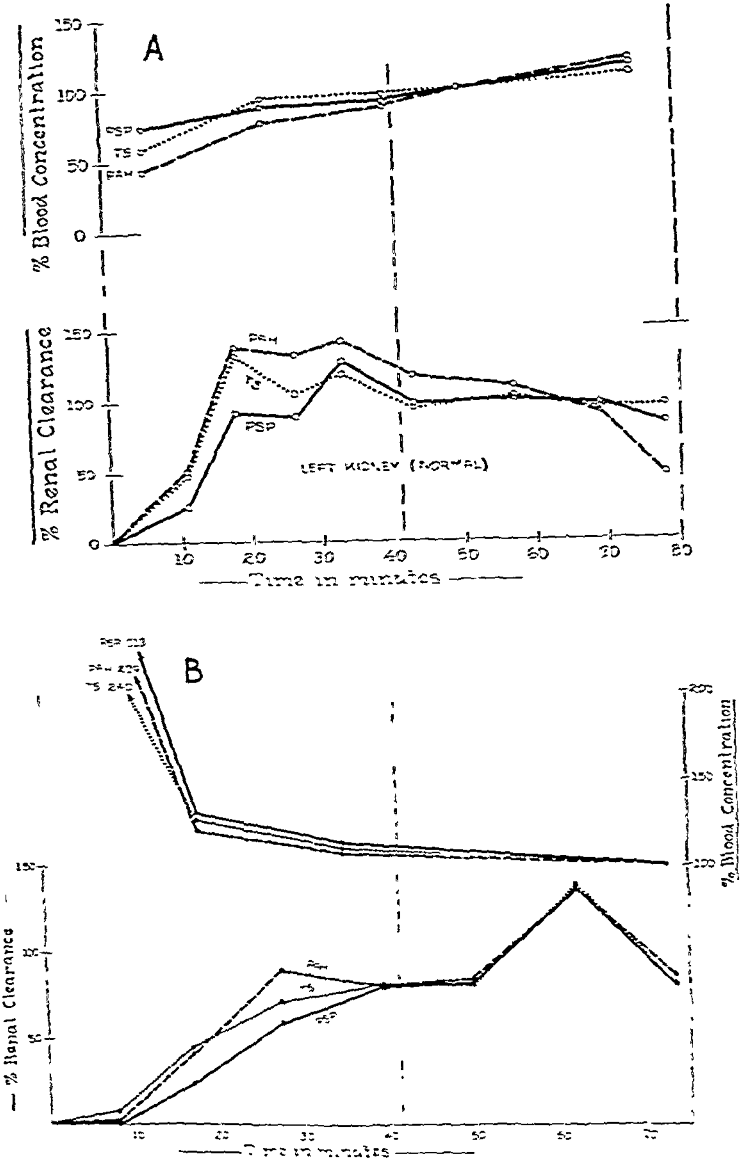

FIG. 2 A, achievement of clearance equilibrium, beyond dotted line, during increasing plasma concentration. Plasma concentrations are plotted at time of collection and clearance values 2.5 minutes before midpoint of urine collection period. *B*, acquirement of clearance equilibrium in a "normal" hypertrophic kidney with falling plasma concentration.

The results have been qualitatively similar to those obtained on normal kidneys. Table 1 summarizes the estimated time intervals after the priming injection required for the clearance to reach 50 per cent of the equilibrium value at constant plasma levels. The similarity of the averages of the test substances, PAH, PSP and M, or TS in normal and pyelonephritic kidneys indicate that the factors responsible for the delay in reaching equilibrium clearance values are intrinsic to the normal kidney and that they are not significantly modified in pyelonephritis.

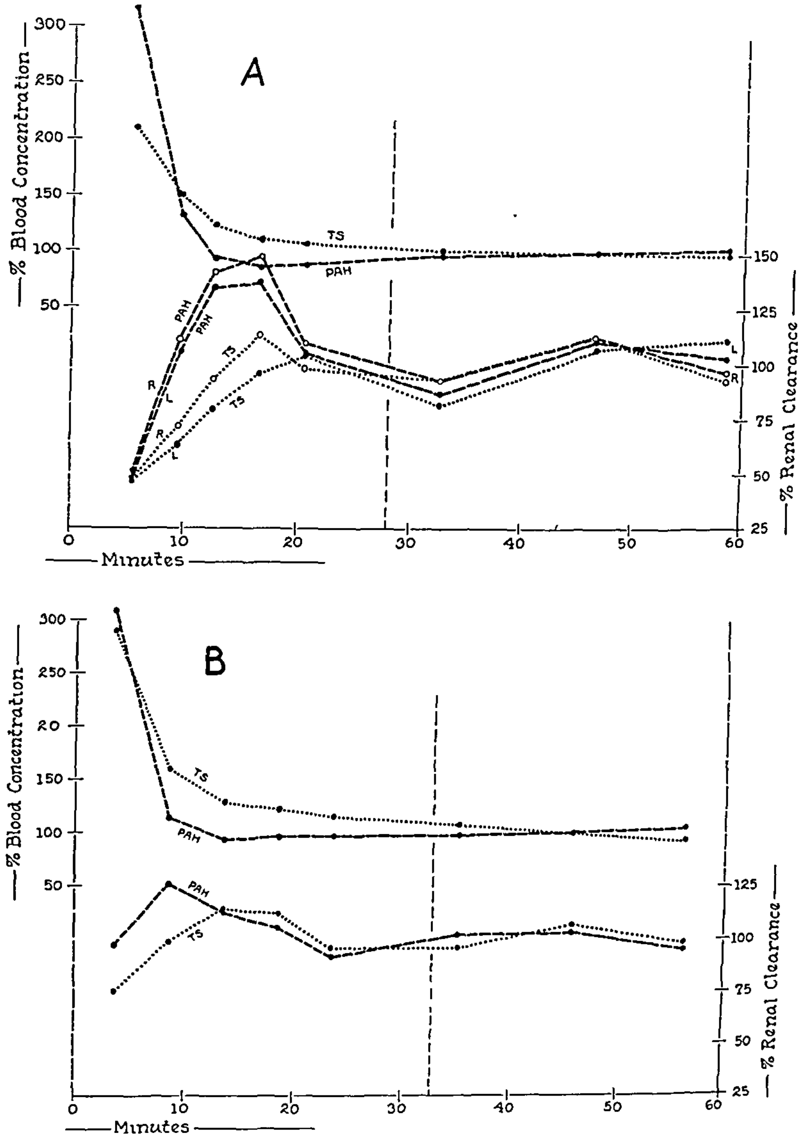

FIG. 3. *A*, arterial plasma concentrations and clearance values are plotted as in figure 2, *A*. Ureteral catheters were used to obtain urine from each kidney. *B*, arterial plasma concentrations and clearance values are plotted as in figure 2, *A*. Urethral catheter used to obtain bladder urine.

TABLE 1. *Clearance equilibrium time at 50 per cent of total clearance*

PATIENT	KIDNEY	PAH	MANNITOL OR TS	PSP	TS-PAH	PSP-PAH
			Normals			
EG	Left	19.0	19.4	24.9	0.4	5.9
MH	Left	10.7	12.6	13.8	1.9	3.1
EM	Right	4.7	5.4	9.3	0.7	4.6
	Left	6.2	6.8	11.6	0.6	5.4
SH	Right	4.3	4.8	11.8	0.5	7.5
KK	Left	11.0	11.1	13.7	0.1	2.7
EG	Left	12.6	15.1	16.6	2.5	4.0
Average		9.8	10.7	14.5	1.0	4.7
			Pyelonephritis			
MS	Right	5.6	6.3	10.3	0.7	4.7
	Left	2.3	3.9	5.5	1.6	3.2
DE	Left	6.0	5.3	8.3	−0.7	2.3
MEH	Left	18.7	19.0	23.5	0.3	4.8
SH	Left	4.4	4.8	13.4	0.4	9.6
KK	Right	13.5	12.0	15.7	−1.5	2.2
Average		8.4	8.6	12.8	1.3	4.5

The estimated time intervals in minutes after the priming injection required for the clearance to reach 50 per cent of the final equilibrium value at constant plasma levels are given for PAH, TS and PSP in columns 1, 2, and 3. The difference as compared with PAH and TS or PSP is shown in columns 4 and 5 respectively.

DISCUSSION

In interpreting the delay in reaching clearance equilibrium the following factors must be considered: *a*) the circulation time from the antecubital vein to the renal arteriole, *b*) the diffusion time from the capillary stream through the renal interstitial fluid, *c*) the penetration and reaction time of the excretory mechanism of the tubule cell, (which includes all phases of energy allocation).[5] and *d*) the dead space time; i.e., the time required for urine formed in the glomeruli to pass to the ureters. It should be noted that factors *b* and *c* do not affect substances excreted solely by glomerular filtration such as TS. The total elapsed time from antecubital vein to the appearance of new urine in the ureter is represented by $a + b + c + d$. This summation will be greater than the first appearance time in so far as the urine, in passing down the tubules, collecting ducts and through the renal pelvis, fails to maintain an unmixed interphase between old and new urine, so that old urine continues to be mixed with new urine at an appreciable time after the first trace of new urine enters the renal pelvis. Moreover, the arrival of new urine at the ureter will *perhaps occur later from long* than from short nephrons, giving the appearance of prolonged mixing.

The fact that the clearance equilibrium time is approximately 20 minutes for required for the clearance to reach 50 per cent of the equilibrium value at constant plasma levels. The similarity of the averages of the test substances, PAH, PSP and M, or TS in normal and pyelonephritic kidneys indicate that the factors

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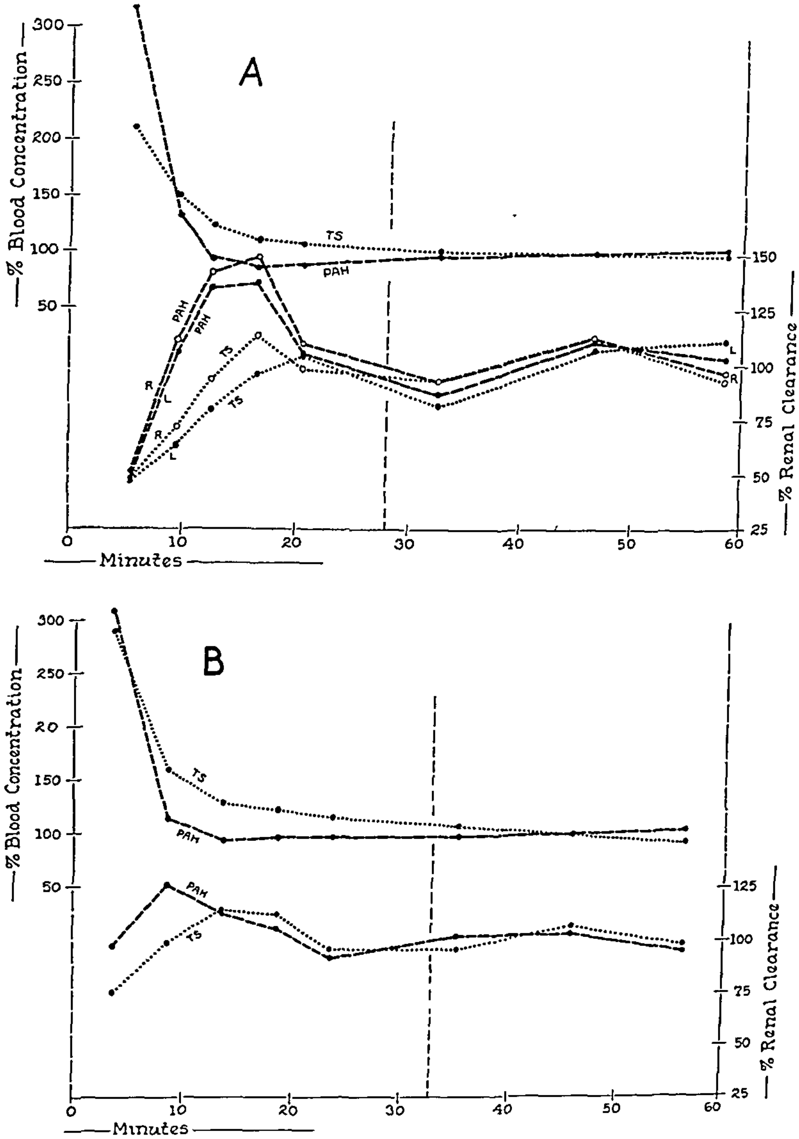
[5] Shannon, J. A., Physiol. Rev., 19: 63, 1939.



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SH	Right	4.3	4.8	11.8	0.5	7.5
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The estimated time intervals in minutes after the priming injection required for the clearance to reach 50 per cent of the final equilibrium value at constant plasma levels are given for PAH, TS and PSP in columns 1, 2, and 3. The difference as compared with PAH and TS or PSP is shown in columns 4 and 5 respectively.

DISCUSSION

In interpreting the delay in reaching clearance equilibrium the following factors must be considered: *a*) the circulation time from the antecubital vein to the renal arteriole, *b*) the diffusion time from the capillary stream through the renal interstitial fluid, *c*) the penetration and reaction time of the excretory mechanism of the tubule cell, (which includes all phases of energy allocation),[5] and *d*) the dead space time; i.e., the time required for urine formed in the glomeruli to pass to the ureters. It should be noted that factors *b* and *c* do not affect substances excreted solely by glomerular filtration such as TS. The total elapsed time from antecubital vein to the appearance of new urine in the ureter is represented by $a + b + c + d$. This summation will be greater than the first appearance time in so far as the urine, in passing down the tubules, collecting ducts and through the renal pelvis, fails to maintain an unmixed interphase between old and new urine, so that old urine continues to be mixed with new urine at an appreciable time after the first trace of new urine enters the renal pelvis. Moreover, the arrival of new urine at the ureter will perhaps occur later from long than from short nephrons, giving the appearance of prolonged mixing.

The fact that the clearance equilibrium time is approximately 20 minutes for

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[5] Shannon, J. A. Physiol. Rev., 19: 63, 1939.

TS,* which is excreted by filtration, as well as PAH which is excreted by the tubules indicates a large magnitude for d, doubtless attributable to the mixing of new and old urine in the tubules and renal pelvis. That the time interval for $a + b + c$ is less than 35 seconds is shown in table 2. In this experiment the priming injection and the constant infusion of the test substances were started at 0 time. Ten seconds after starting the priming injection and at its termination, simultaneous withdrawal of blood from the renal vein and femoral artery was begun. This sample was finished in 50 seconds and is the 0.58 minute (35 second) blood sample recorded in the table. Similar samples are charted at 1.5 minutes, 2.5 minutes, 58 minutes and 90 minutes. The constant extraction of PAH and relatively constant extraction of inulin (used in place of TS) throughout this entire period show that it takes the kidney less than 35 seconds to allocate energy for the effective excretion of these substances. The failure of PAH and inulin to appear in the ureteral urine in a concentration giving a constant clearance must be due to mixing of new-formed with pre-formed urine in the collecting tubules and renal pelvis. It is also apparent that the dead space time is unrelated to the absolute value or the direction of change of the plasma concentration of the test substances and hence the over-all equilibrium clearance time is independent of a rising or falling plasma concentration. It follows that if the plasma concentration is constantly changing, the urine as collected from

TABLE 2. *Renal extraction ratios after a 10 second priming injection followed by a constant infusion*

TIME	FEMORAL ARTERY	RENAL VEIN	EXTRACTION RATIO
	p-Aminohippurate		
Min.	*mgm. %*	*mgm. %*	*%*
0.583	4.50	0.300	93.3
1.50	2.36	0.135	94.2
2.50	1.85	0.105	94.1
58.0	1.23	0.105	91.1
90.0	1.14	0.075	93.0
	Inulin		
0.583	53.3	43.0	19.3
1.50	39.0	30.0	22.6
2.50	32.1	28.0	12.8
58.0	21.7	17.8	18.0
90.0	21.7	17.9	17.5

At "0" time the priming injection of the p-aminohippurate and inulin was started. It was finished and a constant infusion of the same substances started in 10 seconds. Immediately a blood sample was obtained simultaneously over a 50 second period from the femoral artery and renal vein. This is charted at 0.58 minutes (35 seconds), the midpoint of the collection period. Similar samples were obtained at 1.50, 2.50, 58 and 90.0 minutes.

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* Since the correction factor for the analysis of thiosulfate in the presence of p-aminohippurate was less than 2 per cent of the measured value in these experiments, it was not deducted.

the ureter is not related to the simultaneous plasma concentration or even to the plasma concentration corrected for the first appearance time as originally suggested by Smith, Goldring and Chasis,[6] but continues to represent a mixture of old and new urine ambiguously related to the plasma concentration in the 20 minute period before the urine arrives at the ureteral orifice. In the absence of a constant plasma concentration a true or equilibrium clearance will never be attained.

The initial urine volume per minute decreased 50 to 75 per cent in most cases to reach relatively constant values during the clearance equilibrium phase. On theoretical grounds the urine in the renal dead space should be washed out more rapidly at higher urine flows. However, our technique does not permit us to demonstrate this. Clearance equilibrium did not occur in a significantly shorter time in patients with high initial urine flows, 14.7 cc per minute than in patients with low initial flows of 0.25 cc per minute. On the basis of the average urine flow of 2 cc per minute throughout the equilibrating period and an equilibrium time of 20 minutes (52 determinations) the volume of the renal dead space appears to be approximately 2 cc times 20 minutes or 40 cc. If we suppose that 10 or 15 cc of urine are necessary to fill the upper ureter, renal pelvis and calyces, then the volume of fluid in the collecting tubules amounts to 25–30 cc or about 20 per cent of the renal weight.

Under similar conditions the average (V) term for 59 clearance examinations in pyelonephritic kidneys with little or no hydronephrosis is 1.86 cc per minute giving a total dead space volume of 37 cc. Since the dye shadow in the pyelonephritic kidney is usually slightly larger than the normal kidney it is reasonable to assume that the volume of urine in the renal pelvis is perhaps 4 to 5 cc more. Thus, it might take 15 to 20 cc of urine of fill the upper ureter, renal pelvis and calyces of these diseased kidneys. This would give a volume of urine contained in the collecting tubules between 12 and 17 cc.

In both the normal and pyelonephritic kidney the PAH clearance rises and approaches the equilibrium value more rapidly than does TS or PSP. PAH excretion appears to be accelerated about 1 minute ahead of TS. Perhaps the peritubular blood flow is more rapid than the urine flow, so that PAH is available for excretion along the length of the proximal tubule ahead of the simultaneously formed glomerular filtrate, and thus is swept out ahead of the latter. Tubular excretion of PAH from blood passing directly to the renal tubules by way of Isaacs-Ludwig arterioles or *arteriolae rectae verae*, would also lead to this result but the consensus is against the existence of many such vessels in the normal kidney.[7]

Because the tubular excretion of PSP is depressed by raising the plasma concentration of PAH, it is clear that a common mechanism is involved at some stage in their tubular excretion.[5] The difference in clearance equilibrium time may be attributable to differences in the velocity of transport across the tubular cell or to differences in the rate of penetration into the cell. Also, at a plasma

[6] Smith, H. W., Goldring, W. and Chasis, H.: J. Clin. Investigation. **17:** 263, 1938.
[7] Smith, H. W.: J. Clin. Investigation, **20:** 631, 1941.
[5] Unpublished data.

concentration of 2.0 mg. per cent approximately 15 per cent of the PSP is free,[9] whereas 80 per cent of PAH is free.[10] Since only the free compound can diffuse from the capillary into the interstitial fluid, reducing the fraction of the free compound will reduce the diffusion head proportionately. Therefore, in approaching equilibrium clearance a significantly larger fraction of the plasma concentration of PAH may be immediately available to the tubules for excretion than in the case of PSP. Greater availability in the renal interstitial fluid would result in greater excretion at the same plasma concentration but would not prolong the time required for filtration equilibrium to be reached.

SUMMARY

The time required to attain clearance equilibrium after the injection of thiosulfate, p-aminohippurate and phenolsulfonphthalein has been determined in the normal and pyelonephritic kidneys from which urine has been collected by ureteral catheters.

Clearance values and plasma concentrations are not in equilibrium until 20 minutes after starting the infusion leading to constant plasma concentrations. This delay is attributable primarily to the time required to wash out the dead space of the renal tubules and renal pelvis, new urine being mixed with old until the latter is completely replaced.

Where the plasma concentration of any substance is changing significantly, the true or equilibrium clearance cannot be calculated.

PAH reaches equilibrium clearance approximately 1 minute ahead of TS and 2 to 4 minutes ahead of PSP. The physiological implications of these facts have been discussed.

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[9] Smith, W. W. and Smith, H. W.: J. Biol. Chem. **124**: 107, 1938.

[10] Chasis, H., Redish, J., Goldring, W., Ranges, H. A. and Smith, H. W.: J. Clin. Investigation, **24**: 583, 1945.

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DISSOLUTION OF URINARY CALCULI: EXPERIMENTS WITH ETHYLENE DIAMINE TETRA-ACETIC ACID WITH AND WITHOUT A "WETTING AGENT"

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Previous studies have shown that "solution G", a citric acid solution containing magnesium at a pH of 4.0,* readily dissolves certain urinary calculi in which calcium is an important ingredient.[1, 2, 3] These calculi include calcium phosphate stones and stones composed of calcium phosphate and magnesium ammonium phosphate but not calcium oxalate stones. Apparently the calcium in calcium oxalate is too tightly bound to allow rapid dissolution.

At the time these previous investigations were being conducted (1939–1942) experimental work was carried out with calgon, a commercial water softener, which has the property of removing calcium ions from solution. It was found that calgon is likewise a good solvent of calcium-containing calculi and even causes slow dissolution of calcium oxalate stones. It turned out, however, that the prolonged exposure of calgon to rabbit's bladders produces severe irritation, much more than was noted in the bladders of rabbits tested with solution G. Addition of magnesium to calgon did not lessen its irritability.

THE EFFECT OF ETHYLENE DIAMINE TETRA-ACETIC ACID (SEQUESTRINE) ON RABBITS' TEETH AND ON RABBITS' BLADDERS

Our interest in commercial water softeners has continued. Experiments have been carried out with another water softener, ethylene diamine tetra-acetic acid (sequestrine)—produced by the Alrose Chemical Company of Providence, R. I.† Sequestrine has the property of removing from a solution not only calcium ions but also many other cations. Both crude and recrystallized sequestrine were used in solutions of 1 per cent, 2 per cent, and 3 per cent.

From previous studies[1] it has been found that the ability of a solution to demineralize rabbits' teeth grossly parallels its ability to dissolve calcium phosphate stones. Accordingly, each of the above solutions was used as the solvent of rabbits' teeth in groups of eight. The teeth were mechanically shaken in the solvent for eight hours. Their original and final specific gravities were measured,

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* Formula for solution G: Citric acid monohydrate, 32.3 gm.; magnesium oxide anhydrous, 3.8 gm.; sodium carbonate anhydrous, 4.4 gm.; distilled water, ad. 1000 cc.

[1] Suby, H. I., Suby, R. M. and Albright, F.: Properties of organic acid solutions which determine their irritability to the bladder mucous membrane and the effect of magnesium ions in overcoming this irritability. J. Urol., 48: 549, 1942.

[2] Suby, H. and Albright, F.: Dissolution of phosphatic urinary calculi by the retrograde introduction of a citrate solution containing magnesium. New Eng. J. Med., 228: 81, 1943.

[3] Sulkowitch, H. W., Albright, F. and Suby, R. M.: Unpublished data.

† Help with this work was given us by Mr. H. W. Zussman of the Alrose Chemical Company.

and the loss in specific gravity was regarded as the criterion of the efficacy of the solvent.

Table 1 shows the results of sequestrine solutions on 104 teeth. It will be noted that there was no marked difference between crude and recrystallized sequestrine. There was increasing demineralization of the teeth with increasing concentration of sequestrine. The average loss in specific gravity with 2 per cent sequestrine was 0.25 and with 3 per cent sequestrine, 0.30. These are to be compared with figure of 0.29 with solution G. The effect of change in pH was studied with a 3 per cent solution (table 1). However, the data are too few from which to draw a conclusion. It is perhaps noteworthy, nonetheless, that the teeth which lost the least in specific gravity (0.25) were the ones in which the sequestrine solution had the highest pH (6.0).

TABLE 1. *Demineralization of rabbits' teeth in sequestrine solutions*

SEQUESTRINE	pH	LOSS IN SPECIFIC GRAVITY	AVERAGE LOSS IN SPECIFIC GRAVITY
		Crude	
3%	6.03	.26	
	7.00	.25	
		Recrystallized	
1%	—	.16	.13 σ = .04
	4.70	.13	
	4.70	.10	
2%	4.70	.23	.26 σ = .08
	4.70	.30	
3%	4.24	.28	.30 σ = .05
	4.24	.26	
	4.24	.34	
	5.02	.32	
	5.02	.34	
	6.00	.25	

The 1 per cent, 2 per cent, and 3 per cent sequestrine solutions, mostly at a pH between 5.0 and 6.0, were then used as irrigating solutions through two-way catheters into the bladders of rabbits; these bladders were then examined grossly and microscopically. Whereas there was considerable individual variation, there seemed to be considerable irritation, albeit less than with calgon. It was quite evident, furthermore, that the 3 per cent solution is more irritating than the 1 per cent solution.

A solution of sequestrine containing tween (vide infra) at a pH of 4.48 was used to irrigate the kidney pelvis of two patients; each complained at once of pain and the irrigation was stopped. The authors believe that further trials should be made.

THE EFFECT ON RABBITS' TEETH AND RABBITS' BLADDERS OF ADDING A "WETTING AGENT" TO THE SEQUESTRINE SOLUTIONS

Efficiency of solvents such as water softeners can often be increased by substances known as "wetting agents." These have an effect on surface tension and theoretically make solvents get closer to the solute. One of these wetting agents, tween* has been used in 1 per cent, 2 per cent, and 3 per cent concentrations with the 1 per cent, 2 per cent, and 3 per cent sequestrine solutions.

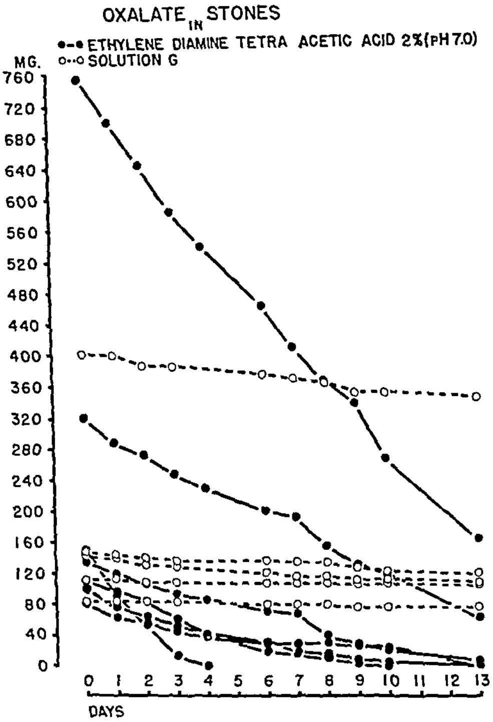

FIG. 1. In vitro dissolution of calcium oxalate stones by ethylene diamine tetra-acetic acid 2 per cent (pH 7.0) and by solution G.

A solution of 1 per cent tween in distilled water at pH 6.12 was found to cause practically no loss in the specific gravity (.01) of rabbits' teeth. Addition of 1 per cent, 2 per cent, and 3 per cent tween to the sequestrine solutions caused no significant increase in loss of specific gravity on rabbits' teeth over plain sequestrine solutions. Tween 1 per cent added to solution G had no effect. Rabbits' bladders irrigated with solutions of sequestrine plus tween showed no more irritation than bladders irrigated with sequestrine alone. In spite of these rather negative results with tween, further work on combinations of dissolving solutions and "wetting agents" is indicated.

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* Tween 80 made by the Atlas Powder Company and is polyoxyethylene (20) sorbitan mono-oleate.

THE EFFECT OF 2 PER CENT ETHYLENE DIAMINE TETRA-ACETIC ACID (pH 7.0) ON OXALATE AND URIC ACID STONES IN VITRO

A series of calcium oxalate and uric acid stones were placed in distilled water for 24 hours, partially dried and weighed. Each stone was then placed in 200 cc of 2 per cent ethylene diamine tetra-acetic acid (pH 7.0) and left at room temperature. At 24 hourly intervals the solution was poured off the stone; the stone was partially dried and weighed; 200 cc fresh ethylene diamine tetra-acetic acid were then added to each calculus. Table 2 shows the losses of each stone in the ethylene diamine tetra-acetic acid. This is depicted graphically in figures 1 and 2.

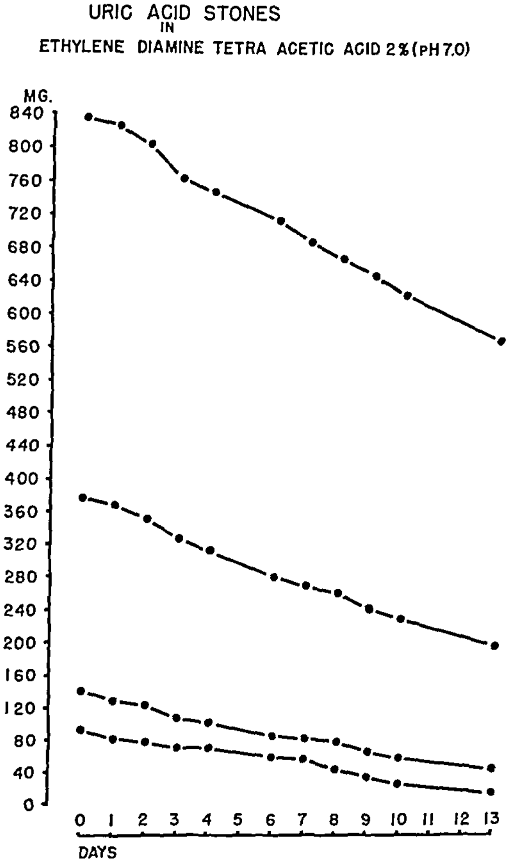

FIG. 2. In vitro dissolution of uric acid stones by ethylene diamine tetra-acetic acid 2 per cent (pH 7.0) and by a watery solution of phosphate (pH 7.0).

In figure 1 it will be noted that ethylene diamine tetra-acetic acid did dissolve calcium oxalate stones at a faster rate than did solution G. The rate of dissolution, however, is much slower than in the case of calcium phosphate stones most of which, under the same technique, are dissolved with solution G within forty eight hours. In figure 2 it will be noted that ethylene diamine tetra-acetic acid does slowly dissolve uric acid stones, but the same results were obtained with a water solution of phosphate at a pH of 7 0

TABLE 2 *Data for figures 1 and 2*

STONE	BEGINNING WT	DAY												
		1	2	3	4	5	6	7	8	9	10	11	12	13
Oxalate Stones in Ethylene Diamine Tetra Acetic Acid 2% (pH 7 0)														
mg	*mg*	*mg*	*mg*	*mg*	*mg*	*mg*	*mg*	*mg*	*mg*	*mg*	*mg*	*mg*	*mg*	*mg*
1	134 3	117 9	106 6	93 4	86 3		71 4	67 5	39 2	27 6	20 5			6 3
2	82 4	62 0	55 2	44 3	37 7		29 1	29 0	30 3	25 8	22 5			0 0
3	98 6	75 5	64 0	50 5	41 1		30 6	18 0	15 7	8 4	4 6			0 0
4	150 2	91 1	53 0	12 7	0 0									
5	754 4	697 2	644 8	584 8	540 0		463 7	410 3	367 3	338 2	267 0			164 2
6	110 8	96 0	83 3	60 2	41 2		18 9	16 2	10 8	3 8	0 0			
7	320 3	287 6	271 6	246 7	229 5		201 2	192 6	155 0	131 8	119 8			61 9
Oxalate Stones in Solution G														
1	84 8	84 6	82 9	82 8			79 8	79 9	79 9	77 3	77 0			76 3
2	112 2	112 5	108 1	109 4			108 7	108 1	108 0	105 6	105 6			105 4
3	401 8	400 2	387 2	386 4			375 6	370 4	365 3	353 1	353 1			346 3
4	142 5	138 6	131 0	128 8			122 0	116 5	115 6	112 1	112 1			108 3
5	148 0	144 1	139 2	137 2			137 4	134 9	134 0	127 1	122 7			119 5
Uric Acid Stones in Ethylene Diamine Tetra Acetic Acid 2% (pH 7 0)														
1	377 1	366 5	351 0	326 8	313 2		279 7	268 9	260 0	241 3	227 6			193 6
2	140 1	128 4	122 4	105 8	101 4		84 1	79 9	74 6	63 7	56 2			41 3
3	836 2	825 8	803 1	761 8	747 0		713 5	687 7	667 3	647 0	623 0			567 9
4	91 6	80 6	76 7	69 3	68 6		58 1	55 0	41 9	31 7	22 8			12 8
Uric Acid Stones in Watery Solution of Phosphate (pH 7 0)														
1	486 0	466 2		410 9		353 9	329 4	305 7	281 6		238 8	220 1	204 2	180 9
2	1197 1	1166 0		1114 9		1043 6	1017 2	988 2	930 7		887 2	848 7	811 3	759 6

DISCUSSION

Gehres[4] and Abeshouse and Weinberg[5] have independently used ethylene diamine tetra-acetic acid for the dissolution of urinary calculi in vitro and in vivo Gehres reported dissolution in vitro of urinary calculi of various chemical compositions Since sequestrine has the property of removing mineral cations from solutions one would expect it to work well with calcium phosphate stones and stones composed of calcium phosphate and magnesium ammonium phosphate Indeed, in the case of the latter mixed stone it should work better than calgon because it removes magnesium ions as well as calcium ions from solutions

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[4] Gehres, R F and Raymond, S A new chemical approach to the dissolution of urinary calculi J Urol 65: 474, 1951

[5] Abeshouse, B S and Weinberg, T Experimental study of a new solvent for renal calculi J Urol, 65: 316, 1951

Just why it should be of help with uric acid stones is not apparent, and this could not be confirmed. The same would hold for cystine stones.

SUMMARY

A solution of ethylene diamine tetra-acetic acid has been found efficacious (in vitro) in demineralizing rabbits' teeth which is an index of the ability of a solution to dissolve calcium phosphate stones.

Ethylene diamine tetra-acetic acid has been found slightly efficacious (in vitro) in dissolving calcium oxalate stones.

Ethylene diamine tetra-acetic acid has been found to be only slightly irritating to rabbits' bladders.

The effect of the addition of a wetting agent (tween) to ethylene diamine tetra-acetic acid on the ability of the latter to demineralize rabbits' teeth has been studied.

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UNUSUAL RENAL TUMORS

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A review of the literature dealing with renal tumors reveals that approximately 95 per cent are malignant and that the majority of these are carcinomas or adenocarcinomas of cortical origin of the type formerly usually designated hypernephroma. There is also evidence that renal tumors fall into two rather distinct age groups: those of infancy and childhood, the majority of which are of mesoblastic origin; and those occurring after middle age, relatively few of which are of this type. The cause of tumors of the kidney in common with those in other locations has remained obscure, necessitating a classification based on the character of tissue from which they arise rather than on the impossible concept of etiology.

In 1948 Culp and Hartman, in an excellent review of the literature concerning tumors of mesoblastic origin in the adult, were able to find 97 acceptable cases and added 4 of their own. They pointed out that of this group of embryonal renal tumors, there were 53 different pathologic diagnoses, most of which had been used in an attempt to describe actual or theoretical features of such tumors. They commented that the resulting confusion in nomenclature has no parallel in either urology or pathology. As a result of this study these authors advocated a logical and simplified classification, the general adoption of which would go a long way toward the abolishment of the existing confusion (fig. 1). If one considers especially those tumors of embryonal cortical origin, they may be grouped under the term mesoblastic nephroma which may be of epithelial, connective tissue, mixed cell types, or undifferentiated (fig. 2).

In applying this classification to a group of 44 malignant renal tumors requiring surgical treatment taken from our files since 1929, there were 25 carcinomas or adenocarcinomas (clear or granular cell), 6 embryonal nephromas of which 3 were mixed tumors (Wilms' type), 2 were undifferentiated embryonal carcinomas and 1 fibrosarcoma, totalling 31 of cortical origin. The remaining 13 cases were epidermoid carcinomas of variable degrees of malignancy of intrapelvic origin. No instance was encountered of a tumor definitely arising from the renal capsule, although this was a possibility with the one fibrosarcoma. Three of these tumors, a mixed cell mesoblastic nephroma in an adult usually referred to as a Wilms' tumor, a term discouraged by Culp and Hartman, a sarcomatous mesoblastic nephroma and an epidermoid carcinoma associated with renal tuberculosis, presented such unusual features that they were considered worthy of more detailed discussion.

As a rule, the diagnosis of tumor involving the kidney is not difficult. One or more of the triad of classical symptoms—pain, tumor, and hematuria—is elicited in taking the history and the subsequent urologic survey usually will reveal

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Read at annual meeting, South Central Section, American Urological Association, Tulsa, Okla. September 26, 1950 abnormal function and outline of the involved organ. Occasionally a Papanicolaou stain of the urinary sediment will be of assistance in establishing a positive diagnosis. There are certain advantages in being able to ascertain preoperatively whether a tumor is of cortical or intrapelvic origin and this has an important practical application in that those having their origin in the renal pelvis or calyces require a complete nephro-ureterectomy. It would be highly desirable if one could determine in advance of surgery whether a tumor is benign or malignant and, if of the latter type, whether it is of renal cell adult type or mesoblastic embryonal origin, having a far more guarded prognosis. Unfortunately, an accurate preoperative diagnosis of the nature of tumors derived from the mesoblast in adults has not been possible. Such tumors may be suspected, however, from the comparatively brief history, rapid growth, the diminished incidence of gross hematuria and the character of tumor cells observed in stained smears of the urinary sediment.

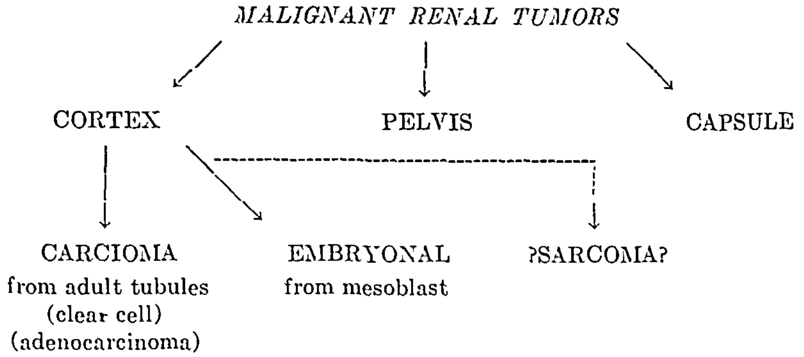

FIG. 1. Chief types of malignant renal tumors. (After Culp and Hartman)

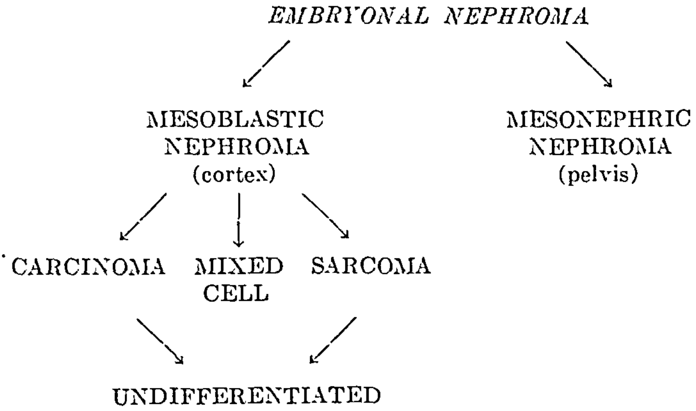

FIG. 2. Classification of embryonal renal tumors. (After Culp and Hartman)

MIXED CELL MESOBLASTIC NEPHROMA IN AN ADULT

This tumor usually has been referred to as a Wilms' tumor occurring most commonly in infancy and childhood. Esersky, Saffer, Panoff and Jacobi in 1947 made a careful review of the literature of this type of tumor in adults and were able to find only 57 cases as of that date including three of their own. Since then Hill has reported 1 case and Silver, 2. The author's case is, therefore, the sixty-first in the literature. Histologically, this tumor is not to be confused with renal sarcoma, which it closely resembles in symptomatology, incidence and degree of malignancy or killing power. One should be able to find carcinoma-like cells in tubular, cylindrical, papillary or solid grouping and also sarcomatous elements which may take the form of oval, round, spindle, or giant cells. The rarity of the lesion is further illustrated by the report of Bell who did not encounter it in the study of approximately thirty thousand necropsy reports. In the group, however, were five Wilms' tumors in children and one renal fibrosarcoma in an adult. The definite diagnosis of mixed cell mesoblastic nephroma in adults is decidedly difficult. The symptoms, signs, and findings on the urologic survey may simulate all other types of renal neoplasms. An unusually large tumor mass is common as is also elevation of temperature unaccompanied by other evidence of a urinary infection, as pointed out by Sparks. He also mentions weakness of the patient out of proportion to the duration of the complaint. Apparently the true nature of the neoplasm has never been diagnosed accurately preoperatively but has been made exclusively by pathologic studies. Approximately 4 out of 5 of the cases reported have occurred in the fourth, fifth, and sixth decades. The treatment is always surgical if the lesion is operable. The prognosis, as in children, is extremely guarded although in a case reported by Loeb in 1949 the patient was living and well 7 years following operation. Alcorn reported patients having lived as long as 7½ to 13 years following nephrectomy.

CASE REPORT

Case No. 51517, Mrs. J. A. M., aged 50, was examined because of gross, painless hematuria which was first noticed seven months previously. This and one other episode of gross hematuria were both of brief duration. Another which began 1 month before had persisted. There were no symptoms referable to the bladder but a moderate degree of discomfort had appeared in the right loin radiating downward and forward. Her general health was good although there had been recent slight loss of weight. On examination there was nothing noteworthy in the physical survey. Neither kidney was palpably enlarged and both were movable. The initial film of the region of the urinary tract was negative as was also the roentgen examination of the chest. The urine was grossly bloody and on cystoscopy the blood was seen to appear from the right ureteral orifice. Stained smears of the urinary sediment were reported negative for tumor cells. Retrograde pyelography disclosed normal outline on the left but on the right there was obliteration of the middle and upper calyces as well as their infundibula, associated with an irregular filling defect along the superior margin of the renal pelvis (fig. 3). The function of the right kidney was markedly impaired on testing with indigo carmine. A diagnosis was made of carcinoma of the right kidney which was thought to be of the intrapelvic type. Exploration was advised including a complete nephro-ureterectomy if the diagnosis were confirmed.

Forty-eight hours after the urologic investigation, the operation was performed with exposure of the kidney through an incision in the loin. The upper half of the organ was definitely enlarged and of dense consistency. It was possible to approach the renal pedicle with a minimum of manipulation and clamps were applied early. Mobilization was then completed including the upper ureter which was severed and the stumps immediately electrocoagulated. Removal of the organ was without incident. It was immediately sectioned, revealing an extensive neoplasm involving the upper half, whereupon the remainder of the ureter was mobilized as far as could be reached after ligating the electrocoagulated proximal end. With the patient in the recumbent posture an extraperitoneal approach was made through a split muscle incision to the lower third, permitting the removal of the ureter in its entirety, including a segment of the bladder. The patient made an uneventful convalescence. Both incisions healed by primary intention and she was dismissed on the eighth postoperative day. Three months later her examination, including cystoscopy and roentgen study of the chest, was negative. In answer to a recent inquiry it was reported that she considered herself in good health and doing her usual household duties fourteen months following the nephrectomy.

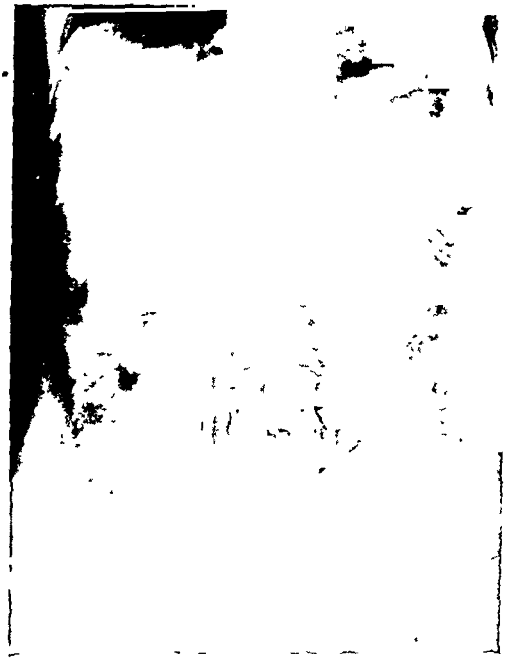

Fig. 3. Bilateral retrograde pyelograms. Right, note irregular filling defect of pelvis and obliteration of upper calyces from tumor. Left, normal.

Pathologic report. "This specimen is submitted as a right kidney and right ureter. It measures 11.5 cm. in length by 6 cm. in width and 5.5 cm. in thickness and weighs 210 gm. In one point of the kidney lies a bulbous enlargement which feels tense to the touch. On section the kidney is seen to contain some tissue which has a brawny consistency and has replaced the normal architecture in the upper two-thirds (fig. 4). The cortex in this region is thinned to 0.2 cm. at its thinnest point. The average thickness of the cortex is approximately 0.4 cm. This mass of tissue is yellowish-white in color with hemorrhage in several areas. The tumor mass in the second portion of the kidney seems to lie within the cavity lined with mucosa from the pelvis. This capsule is distended to the cortex and there is no remaining parenchyma. There is a great deal of difference in consistency in various portions of the tumor mass. That portion described as a bulbous enlargement at the upper pole is much more firm than any other tissue found in that part of the kidney. The second portion of this specimen which

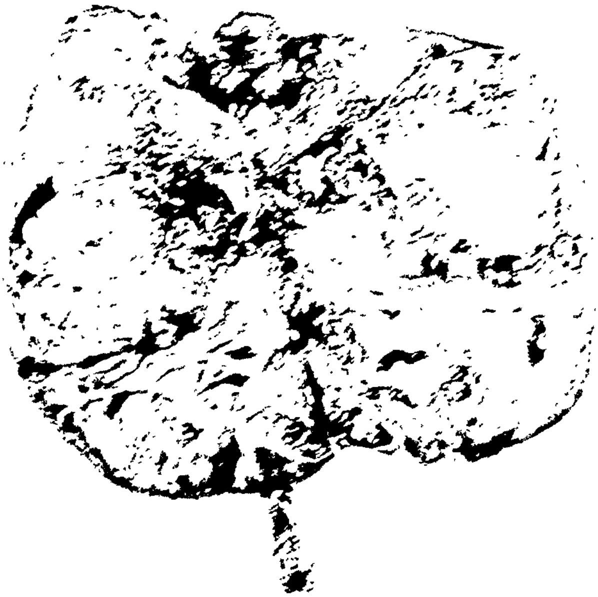

Fig. 4. Mixed cell mesoblastic nephroma in an adult (Wilms' tumor).

was submitted as a ureter measures 16 cm. in length and 0.5 cm. in average diameter. On one end of the elongated structure there is a mass of tissue which appears to have been electrocoagulated. At the other end there is bulbous dilatation where the structure attains a diameter of approximately 0.6 cm. This area is soft in consistency. The lumen is patent throughout."

Microscopic report. (See figure 5.) "The bulk of this lesion consists of small, spindle-shaped cells with scant cytoplasm growing in interweaving bundles. Their nuclei have a fusiform shape, are hyperchromatic, and contain occasional mitotic figures. Scattered irregularly within this picture are distinct epithelial structures around which the other tumor component is concentrically arranged. The epithelial-like tissue consists of several to numerous poorly formed glandular structures with lumens lined by plump, cuboidal epithelium. These duct-like structures merge with each other, and some fail to develop a lumen. Their cells have scant, pink cytoplasm and are largely occupied by a nucleus. These nuclei vary twofold in size and shape. Around the periphery of this tumor is a thick zone of fibrosis which separates it from the adjacent compressed and atrophic kidney parenchyma.

Diagnosis: Mixed cell mesoblastic nephroma (Wilms')."

Comment. Unlike the majority of tumors of this type, the mass was comparatively small. It will be noted that the neoplastic cells comprised a mixture both sarcomatous and carcinomatous. Occasionally one may find a distinct carcinoma and sarcoma in the same organ which should be regarded as multiple tumors rather than a mixed one. The persistent gross hematuria of approximately one month's duration is unusual for this type of neoplasm. It is unfortunate that numerous stains of the urinary sediment failed to reveal characteristic tumor cells which might have permitted accurate preoperative diagnosis for the first time in this type of renal neoplasm.

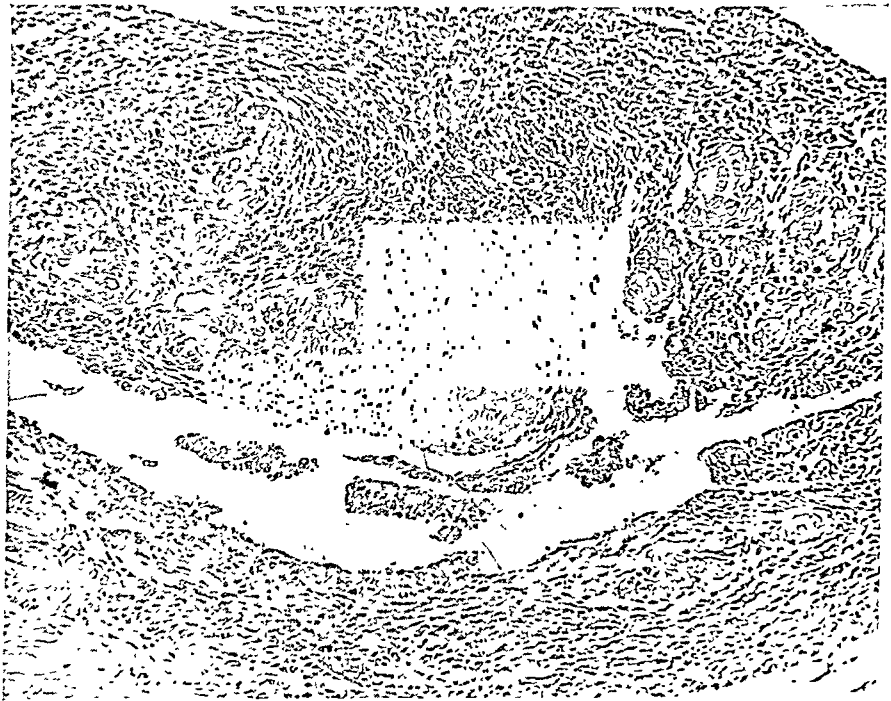

FIG. 5. Low power photomicrograph; note small spindle-shaped cells in intertwining bundles and scattered epithelial structures which did not stain well.

RENAL FIBROSARCOMA

Although the true nature of tumors derived from the mesoblast in adults has not been possible to diagnose before operation, such tumors should be suspected from the comparatively brief history, rapid growth, the diminished incidence of gross hematuria and the character of tumor cells observed in stained smears of the urinary sediment. In 101 instances of mesoblastic nephroma collected from the literature by Culp and Hartman, including 4 of their own, 35 were fibrosarcomas. The rarity of such tumors is indicated by the report of Weisel, Dockerty and Priestley who found that 35 had been treated surgically at the Mayo Clinic from 1904 to 1940 inclusive, an incidence of approximately only 1 in 30,000 patients examined at this institution. Microscopically, the lesions were basically composed of spindle cells resembling fibroblasts and were accordingly judged to be fibrosarcomas. All of them appeared histologically to be of a relatively high degree of malignancy: 90 per cent could be graded 3 or 4. These authors suggest the abandonment of such descriptive terms as small round-cell sarcoma, spindle cell sarcoma, and giant cell sarcoma as many of these oval, round, spindle or giant cell forms are merely anaplastic variants of a single cellular type and do not represent individual or separate entities. The extremely poor prognosis with this type of tumor is evidenced by the fact that of this group only 5 living patients could be traced, one of whom was suffering from recurrence 18 months after nephrectomy and 4 had survived and were apparently well postoperatively for periods of 1, 2, 4, and 11 years.

Renal sarcoma is not to be confused with mixed cell mesoblastic nephroma: the latter is a mixed neoplasm containing both connective tissue and epithelial elements of mesodermal origin. Kretschmer and Randolph state that true renal sarcoma is a disease not of children but of adults. Only at the surgical exploration may the true nature of the neoplasm be disclosed. It may comprise a yellowish solid mass which nearly always involves some portion of the renal capsule. Areas of hemorrhage are common. The microscopic pattern is variable and easily confused with other types, especially undifferentiated adenocarcinoma. In a case report by Henline, although an extension of the tumor was removed from the vena cava, the patient was alive and well $3\frac{1}{2}$ years later. Such an experience serves to encourage nephrectomy whenever possible in spite of the extremely poor ultimate outlook.

CASE REPORT

Case No. 46395. J. B. I., a man aged 61, was examined primarily because of symptoms of prostatism which had been slowly progressive over a period of 10 years. There was nocturia of 4 to 5 times and the symptoms had become especially troublesome during the previous month. He had experienced recently dull pain in the lower lumbar region along with some minor digestive disturbances. There had been no loss of weight, fever nor gross hematuria. The prostate gland was found to be moderately enlarged of benign type and there was 225 cc of infected residual urine. A transurethral prostatic resection was performed, with the removal of 31 gm. of tissue, which was reported by the pathologist as benign prostatic hyperplasia. His immediate convalescence was satisfactory and upon removal of the inlying catheter on the third day he was able to empty the bladder completely and with normal control. About this time he began to complain of an increasing degree of discomfort in the left loin associated with a mass which had not been noted at his original examination and was thought to be possibly an enlarged spleen. Excretory urography, however, disclosed that the left kidney was without function and on passage of a ureteral catheter, 30 cc of thick pus was aspirated from the left renal pelvis. Retrograde pyelography failed to reveal a deformity characteristic of a renal tumor (fig. 6), but the dense mass in the region of the lower pole appeared to be connected with the kidney, which it accompanied on movement with respiration. Roentgen studies revealed no evidence of metastases. *The preoperative diagnosis* was left pyonephrosis associated with a left renal tumor. Three weeks following the transurethral prostatic resection, the kidney was explored and presented the appearance of a typical pyonephrosis in combination with a hard nodular tumor involving the lower pole and rather loosely attached to the peritoneum over the anterior aspect. A nephrectomy was performed without incident after which the immediate convalescence was satisfactory and he was dismissed from the hospital on the nineteenth postoperative day.

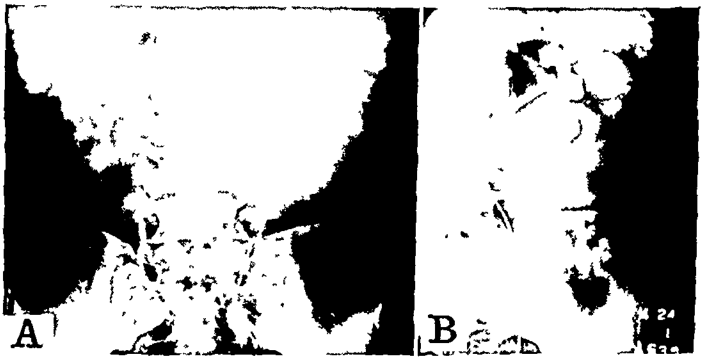

FIG. 6. *A*, excretory urogram. Note absence of function, left. Right, normal. *B*, left retrograde pyelogram revealing pyonephrosis and mesial displacement of upper ureter by large mass at lower pole.

Although he was able to be up and about and appeared to be steadily regaining strength, his condition was progressively downhill upon his return home and his death was reported 14 days later or 32 days postoperatively. A postmortem examination was not made and the immediate cause of death was not determined.

Pathologic report. "The left kidney measures 18 by 12 by 7 cm. and weighs 600 gm. There is a large deposit of fatty tissue which appears to be inflammatory. The lower pole presents a tumor mass measuring 12 cm. in diameter, and occupies more than two-thirds of the parenchyma. The cut surface is glistening, yellowish-white, and appears to be undergoing some myxoid changes. The edge of the growth which invades the parenchyma is lobulated and tends to be elevated above the cut surface. The remaining pelvis is dilated and distorted. The upper pole presents a hemorrhagic cyst 3 cm. in diameter and a number of soft yellowish-white areas which have the appearance of abscess cavities."

Microscopic report. (See figure 7.) "Sections through this lesion reveal a uniform picture of closely packed spindle-shaped cells almost completely replacing renal tissue. The limits between this tumor and the adjacent renal parenchyma are sharply defined although there is no surrounding capsule. The tumor itself is made up of slender, fusiform cells with long axes that are generally parallel to each other. The cells do not attempt to form bundles. Cell outlines are fairly distinct with their central portions containing a nucleus. These nuclei are ovoid and vary threefold in size and shape. There are occasional mitotic figures. The section taken near the renal pelvis reveals marked infiltration of neutrophils and lymphocytes.

Diagnosis: Renal fibrosarcoma; pyonephrosis."

Comment. This case is of unusual interest inasmuch as the patient was admitted to the hospital for relief of benign prostatic obstruction and during his convalescence from a transurethral prostatic resection and while under daily observation, the symptoms and signs of the left renal tumor rapidly appeared and were regarded as chiefly attributable to pyonephrosis. There was no gross hematuria other than that usually seen after a transurethral resection. The main evidence of renal tumor was the rapidly growing, palpable, indurated mass at the lower pole of the kidney unaccompanied by the usual pyelographic deformity of a renal neoplasm. Not until the exploration was the presence of a sarcoma definitely ascertained, the true nature of which awaited the pathologist's report. It might have been suspected, however, if due attention had been paid to the typically brief history, rapid growth of the tumor, and absence of gross hematuria. The patient's early demise is characteristic of the highly malignant nature of the disease.

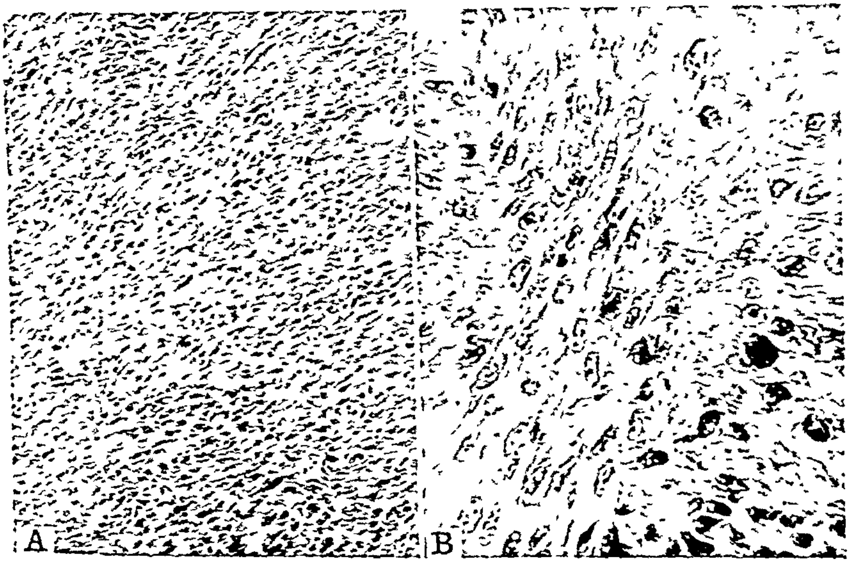

Fig. 7. Renal fibrosarcoma. *A*, low power photomicrograph. Note closely packed spindle-shaped cells. *B*, high power photomicrograph. Note slender fusiform cells with long axes and nuclei in their central portions.

ASSOCIATED MALIGNANCY AND TUBERCULOSIS OF THE KIDNEY

The association of carcinoma or sarcoma with tuberculosis involving the same kidney is of such unusual occurrence that it merits special consideration. Neibling and Walters in 1948 reviewed the literature and were able to collect 26 cases of combined renal tuberculosis and hypernephroma although in one of these reported by Keen in 1934 right renal tuberculosis was associated with a hypernephroma in the opposite kidney and perhaps should not have been included. These writers added 7 additional cases, 4 of which were considered primarily tuberculous and in 2 a renal neoplasm was diagnosed. After an analysis of 7500 autopsy reports, Pearl was of the opinion that an antagonism existed between active tuberculosis and carcinoma. Carlson and Bell, in a series of 11,195 necropsies, found active tuberculosis less common in cases of carcinoma. They did not think, however, that an antagonism actually existed. MacDonald in 1947 found two additional cases in the literature of renal sarcoma associated with tuberculosis (Pepe 1938; Suzuki 1941) and added a case of his own of hypernephroma coexisting with tuberculosis. Puigvert and Anguera in 1948 added 2 cases of papillary epithelioma and tuberculosis and also mentioned a case reported by Marion in 1912 and a case reported by Chevassu in 1934, the latter 2 cases apparently having not been mentioned in reviews of the literature by other authors. The accumulated cases referred to totaled 32 to which I would like to add a case in which not only was there an epidermoid carcinoma associated with tuberculosis but there was a stone in a tuberculous cavity of the kidney in addition to hydronephrosis and chronic pyelonephritis—a veritable pathologic museum.

CASE REPORT

Case No. 40542, Miss L. M., aged 58, was first seen May 10, 1934, because of a moderate degree of urinary frequency which had gradually progressed during the previous 2 or 3 years. Upon finding a considerable degree of pyuria, her physician had referred the patient for a urologic investigation. The initial roentgenogram disclosed an irregular shadow approximately 2 cm. in diameter in the region of the lower pole of the left kidney (fig. 8, *A*). Cystoscopic examination disclosed a moderate degree of chronic granular urethritis with extension of the inflammatory process onto the trigone. The bladder capacity was only 8 ounces. Phenolsulfonphthalein appeared after 3 minutes from each kidney with an excretion of 24 per cent from the right and 16 per cent from the left in 15 minutes. Urinalysis of the right renal specimen was negative, whereas the specimen from the left contained an average of 6 pus cells per high power field; a stained smear revealed no acid fast bacilli nor were other bacteria noted. Pyelography revealed a normal outline on the right but the shadow in the left renal area filled a cavitation at the lower pole which communicated with the lower calyx, suggesting the possibility of stone formation in a tuberculous cavitation (fig. 8, *B*). Exploration of the kidney was advised with the view of resection of the lower pole, which the patient refused. She was seen at irregular intervals because of the persistent pyuria and symptoms of a moderate degree of cystitis. She seemed content to tolerate the complaint rather than undergo surgical treatment.

After a period of 14 years she began to complain of moderate discomfort in the left upper abdominal quadrant first thought to be of intestinal origin. Later the discomfort was noted more posteriorly and her physician requested another urologic study. Roentgen examination disclosed that the shadow previously mentioned was essentially unchanged in size or position. Cystoscopy revealed a fairly diffuse degree of chronic inflammation, more marked in the region of the trigone. The spurts from the right orifice were clear and were cloudy from the left. Indigo carmine returned in deep concentration after 4 minutes from the right and did not appear from the left after 10 minutes. After ureteral catheterization 22 cc of cloudy urine was aspirated from the left, containing grade 2 concentration of indigo carmine and innumerable pus cells. The specimen from the right was negative. The right pyelogram was normal. The left revealed pyelectasis, grade 2, with evidence of an obstructive factor at the ureteropelvic juncture. When compared with the pyelogram made 14 years previously, changes involving the upper pole were in evidence in that it had become foreshortened and broader (fig. 8, *C*). Studies for acid fast bacilli were again negative. Exploration of the kidney was again advised and accepted.

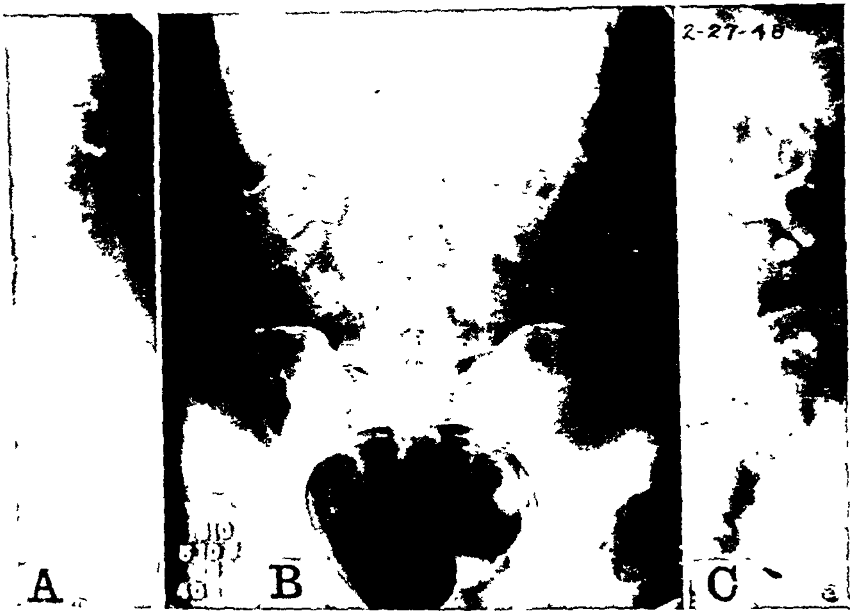

FIG. 8. *A*, initial film revealing irregular shadow in left renal area. *B*, excretory urogram. Note normal function and outline, right, moderately diminished function, left, with inclusion of shadow in cavitation at lower pole adjacent to lower calyx. *C*, left retrograde pyelogram obtained 14 years later. Note persistence of stone in cavitation at lower pole, moderate pyelectasis and striking change in outline of upper calyx from tumor.

Under subarachnoid block the kidney was exposed through an incision in the left loin and was easily mobilized and the cortical stone at the lower pole was palpable through the thinned cortex overlying it. An indurated area about 3 cm. in diameter was noted near the upper pole on the anterior aspect, having a grayish appearance on the external surface. It appeared to be neoplastic rather than inflammatory. The ureter was moderately thickened, was doubly clamped and divided about 5 cm. below its junction with the pelvis with electrocoagulation of the stumps. The kidney was removed without incident. Her convalescence was satisfactory and she was dismissed on the fourteenth postoperative day.

One month following the operation she was readmitted to the hospital because of severe pain in the lower lumbar spine requiring opiates for relief. The pain gradually increased in severity and subsequent roentgen studies established the diagnosis of multiple spinal metastases. Roentgen examination of the chest at no time revealed evidence of tuberculosis or metastatic lesions from the neoplasm. The patient expired at home five months following the nephrectomy. A necropsy was not performed.

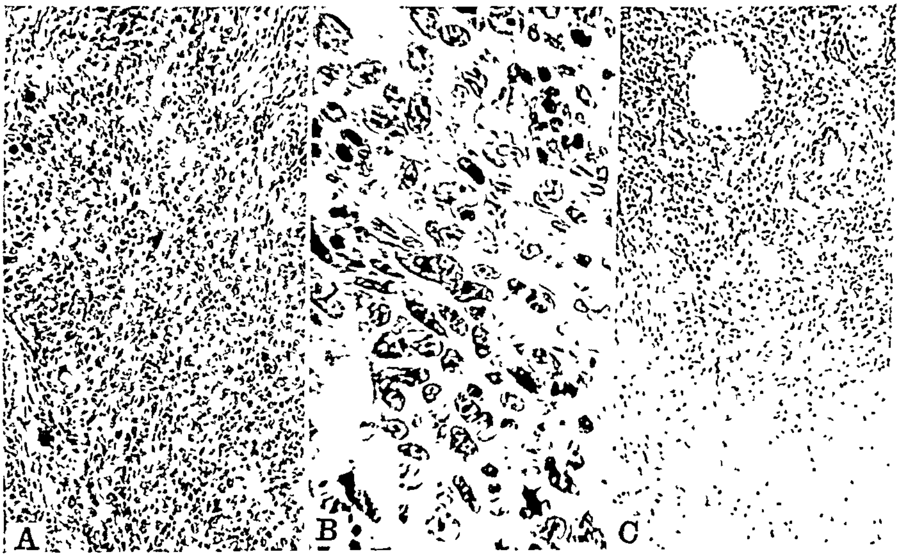

FIG. 9. *A*, low power photomicrograph; note area of epidermoid carcinoma and surrounding inflammatory zone of chronic pyelonephritis. *B*, high power; note poorly differentiated carcinoma cells. *C*, low power; note typical picture of tuberculosis, including giant cell and area of necrosis.

Pathologic report. "The specimen consists of a kidney which measures 13½ by 6½ by 4¼ cm. On its external surface, at the upper pole of the kidney, is an indurated area measuring 4½ by 3 by 2 cm. On section there is a firm granular, nodular tumor formation which has undergone some degree of degeneration. There is palpated in the pelvis several irregular stones. Longitudinal section through the kidney reveals the pelvis to be moderately dilated. The cortex and medulla are somewhat thinned. At the lower pole there are two stones embedded in the cortex of the kidney. The largest of these measures approximately 2 cm. in its greatest diameter. There is also noted within the pelvis of the kidney numerous small stones measuring approximately 1½ to 2 mm. in size. At the site previously described on the external surface there is noticed a firm extension of tumor growth on the cut surface of the kidney."

Microscopic report. (See figure 9.) "Multiple sections through this kidney reveal several distinct processes. One is an epidermoid carcinoma extending from the renal pelvis rather deeply into the kidney substance. This tumor is growing as broad anastomosing sheets and cords of moderately undifferentiated keratinized epithelium. The tumor cells are relatively large with indistinct cytoplasmic outlines. The abundant cysstoplasm is homogeneous and pink, consistent with keratin. Their nuclei vary fourfold in size and shape, are moderately chromatic, and show frequent mitotic figures, many of which are bizarre. Another distinct lesion is tuberculosis manifested by scattered, discrete, granulomatous lesions. Most of the larger ones show principally a central caseous, amorphous mass surrounded by marked number of lymphocytes, some epitheloid cells, and occasionally considerable fibrosis. Langhans' cells are occasionally seen. In the smaller lesions there are numerous epitheloid cells arranged radially in a thick zone surrounding central necrosis. Elsewhere in the renal parenchyma is considerable diffuse, lymphocytic infiltration of the interstitial tissue, and this reaction appears removed and distinct from the tuberculous change. Glomeruli are frequently completely hyalinized, and there is much atrophy and loss of tubules. Changes in the vascular walls are not remarkable.

Diagnosis: Epidermoid carcinoma, grade 3; renal tuberculosis; nephrolithiasis; hydronephrosis; chronic pyelonephritis."

Comment. Undoubtedly the kidney became involved with tuberculosis in comparatively early life as when the patient was first seen 14 years previously, the cavitation at the lower pole was snugly filled with stone. Apparently the disease remained limited to this area over the long period of years and at no time was she troubled with a severe degree of secondary tuberculous cystitis so commonly experienced in the presence of renal tuberculosis. The highly malignant epidermoid carcinoma was probably of recent origin arising in an area near the upper pole quite distant from the tuberculous process. If antagonism actually exists between malignancy and tuberculosis as has been suggested, the latter disease failed to protect the organ from carcinoma and thus tends to refute the idea. Although the neoplasm was comparatively small, the histologic picture gave definite evidence of an almost total absence of differentiation and its highly malignant nature. The period of survival, however, was much shorter than was anticipated at the time of surgery.

SUMMARY

The reports of three unusual renal neoplasms are submitted in abstract. The first of these, a mixed cell mesoblastic nephroma (Wilms' tumor) in an adult is the sixty-first reported in the literature. The second case, a renal fibrosarcoma, apparently is the one hundred third case reported. The third case of a malignancy associated with tuberculosis involving the same kidney is the thirty-third to be recorded in the literature.

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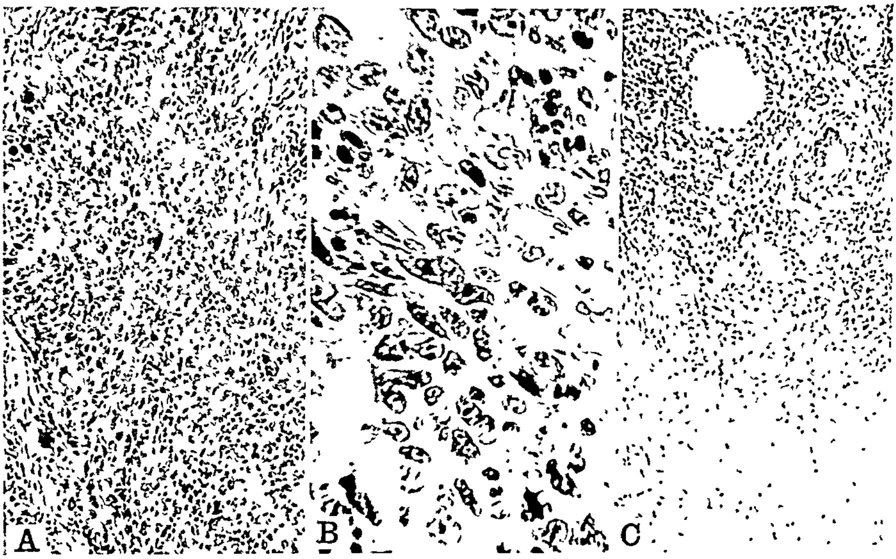

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REFERENCES

Alcorn, K A Wilms' tumor in an adult Proc Staff Meet Mayo Clinic, **12:** 692–694, 1937

Bell, E T A classification of renal tumors with observations on the frequency of the various types J Urol , **39:** 238–243, 1938

Carlson, H A and Bell, E T *A statistical study of the occurrence of cancer and tuberculosis* in 11,195 postmortem examinations J Cancer Res , **13:** 126, 1929

Chevassu (Quoted by Puigvert and Anguera)

Culp, O S and Hartman, F W Mesoblastic nephroma in adults A clinicopathologic study of Wilms' tumors and related renal neoplasms J Urol , **60:** 552–576, 1948

Eserskey, G L , Saffer, S H , Panoff, C E and Jacobi, M Wilms' tumor *in the adult* Review of literature and report of three additional cases J Urol , **58:** 397–411, 1947

Henline, R B Fibrosarcoma of a polycystic kidney with extension into vena cava Report of case with successful surgical removal J Urol , **39:** 238–243, 1938

Hill, R M Embryoma of the kidney in the adult Brit J Urol , **18:** 53–59, 1946

Keen, M R Associated renal tuberculosis and malignancy Am J Surg , **25:** 467–475, 1934

Kretschmer, H L and Randolph, H S *Spindle celled sarcoma of the kidney in adults* Ann Surg , **88:** 1033–1038, 1928

Loeb, M J Report of postoperative survival of two cases of malignancy (1) Carcinoma of the adrenal cortex, (2) Wilms' tumor in an adult J Urol , **61:** 20–22, 1949

MacDonald, S A Co existing hypernephroma and tuberculosis Can Med Assn J , **57:** 572–575, 1947

Marion (Quoted by Puigvert and Anguera)

Neibling, H A and Walters, W *Adenocarcinoma and tuberculosis of the same kidney* Review of the literature and report of seven cases J Urol , **59:** 1022–1035, 1948

Pearl, R Cancer and tuberculosis Amer J Hyg , **9:** 97, 1929

Pepe (Quoted by S A MacDonald)

Puigvert, A and Anguera, A O Cancer and tuberculosis in the kidney Urol & Cutan Rev , **52:** 441–448, 1948

Silver, H K Wilms' tumor (embryoma of the kidney) J Pediat , **31:** 643–650, 1947

Sparks, A J Wilms' tumor in sixty-three year old male Case report J Urol , **47:** 642–647, 1942

Suzuki (Quoted by S A MacDonald)

Weisel, W , Dockerty, M B and Priestley, J T Sarcoma of the kidney J Urol , **50:** 564–573, 1943

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SIMULTANEOUS WILMS TUMORS IN IDENTICAL TWINS

EUGENE GAULIN

Since Max Wilms' remarkable monograph on embryonal adenomyosarcoma of the kidney published in 1899, an impressive number of malignant mixed tumors of the renal parenchyma have been reported in the medical literature.

Kretschmer and Hibbs, Hinman and Kutzmann, Mixture, Prather and Crabtree, Dean and Pack, Priestley and Broders, Campbell, Ladd and many more authors have scrutinized extensively the clinical, pathological and therapeutic aspects of this dreadful disease. Although this condition remains one primarily affecting children, the literature has gathered nearly one hundred cases found in adults.

Walker, Deuticke, Bobbio and Maslow have reported cases of embryoma appearing in children of the same family. Kretschmer and Hibbs, Ladd, and Campbell reported cases of bilateral adenomyosarcoma. To our knowledge, no mention has been made as yet of Wilms tumors occurring simultaneously in identical twins. It has been our privilege to see this rare condition and it is the object of this report.

CASE REPORTS

Case 1. Robert, aged 15 months, was admitted to the Ottawa General Hospital March 27, 1946. The baby was brought to the hospital because "he was pale, cried more than usual and was losing weight." The family history was irrelevant. The child was born at full term; birth weight, 5 pounds. His appetite had always been good until about 2 weeks before admission.

Physical examination revealed an anemic, sick looking child, slightly under weight and presenting a distended abdomen. A solid, hard mass filled the left side of the abdomen, and extended from the left costal arch to the iliac fossa. The left flank was bulging outward and the bowels were displaced mesially. The temperature was 99.4F. The urine was negative for pus and blood; albumin, 1 plus; hemoglobin 25 per cent, erythrocytes, 4,000,000; white blood cells 8,000. An excretory urogram revealed a good right kidney and a functionless left kidney. Screening of the lungs was negative for metastases. Numerous transfusions of whole blood were given and the blood picture improved rapidly.

Operation was performed on April 5, 1946. Through a posterolateral approach the kidney was removed with great difficulty. The surrounding structures were very adherent to the tumor which had broken through its capsule. The pedicle formed a solid mass, cartilage-like. Postoperatively, the child was shocked and in spite of supporting drugs and transfusions, he died the following day.

Pathological report: The specimen was a large, nodular, irregular-shaped tumor weighing 2 pounds, 2 ounces. It was surrounded in part by a thick capsule of fibro-fatty tissue which was white and hemorragic. There was no resemblance at

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Read before joint meeting, Western New York and Ontario Urological Society and the Central Section, American Urological Association, Seigniory Club, Province of Quebec Canada, October 14, 1948.

all to a kidney. The tumor had been opened up and showed shaggy masses of hemorragic tissue with nodular masses of white tissue, in appearance neoplastic. In blocks from different portions of this tumor, at low-power, immature epithelial clumps were evident in a background of loose undifferentiated primitive connective tissue. High-power view: Attempted tubule formation was seen in the upper clump. Diagnosis: Wilms tumor (fig. 1, *A* and *B*).

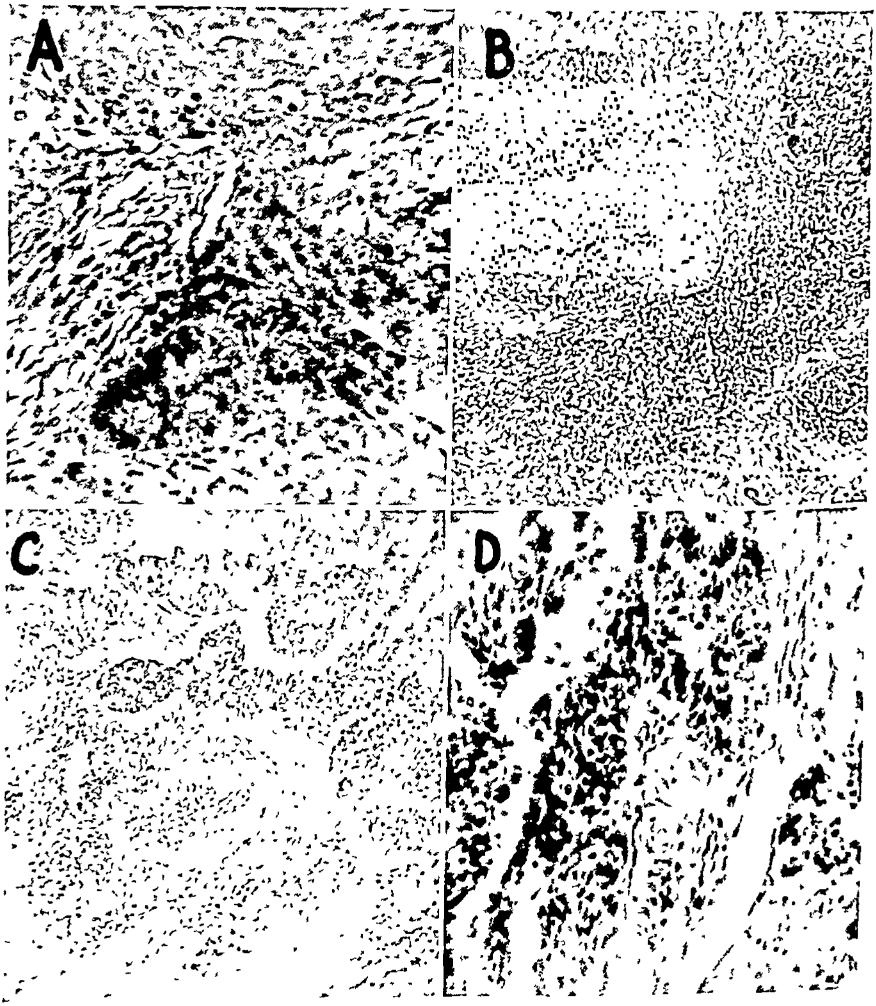

Fig. 1.

Case 2. Albert S., aged 15 months, was admitted to the Ottawa *General Hospital* March 27, 1946, because "he was pale, cried more than usual and was losing weight." The child was born at full term, birth weight $4\frac{1}{2}$ pounds.

Physical examination revealed an anemic infant weighing 18 pounds. The abdomen was greatly distended. The swelling filled the right side of the abdomen from the right hypochondrium to the iliac fossa. The right flank bulged outward. The mass was hard and nontender. The temperature was 100F. The urinalysis showed 3 plus albumin, otherwise negative; hemoglobin, 48 per cent; erythrocytes, 3,840,000; white blood cells 9,600. Numerous transfusions were given and on April 29, the hemoglobin reached 75 per cent. X-ray films of the chest were negative for metastases. An excretory urogram revealed a good left kidney and total absence of function of the right.

Operation was performed on May 4, 1946, by means of a posterolateral curved incision. The tumor was totally adherent to the surrounding structures. The pedicle was hard, pearly white, thrombosed. The patient made an uneventful recovery and was discharged May 25, 1945. He died 3 months later with a recurrence in the wound.

Pathological report: The specimen was a large tumor, weighing 2 pounds. It had little resemblance to a normal kidney. On section there was a large central cystic mass filled with blood clots. The rest of the tissue was neoplastic in appearance. In the low-power microphotograph of this renal tumor, one saw sheets of mesenchyme-like connective tissue in which were clumps of incompletely differentiated epithelial cells. There was a suggestion of tubule formation in a few areas. On high-power view, the immature epithelial elements were well seen. Diagnosis: Wilms tumor (fig. 1, *C* and *D*).

DISCUSSION

The parents, aged 32 and 30 respectively, are healthy, living on a farm. They have been married 5 years and have 2 healthy children living. The twins were born healthy, full term deliveries. They were well fed and received an adequate diet. Without a doubt, they were identical twins. The doctor who delivered the mother is sure of a common placenta. They became ill at the same time, were admitted to the pediatric service on the same day with an identical history. They showed the same clinical picture. The abdominal masses were identical except that one occupied the right side of the abdomen and the other the left side. The blood picture was low and quite similar in both twins. They were both in blood group A, Rh positive, Wassermann negative. Excretory urography showed a functionless kidney in both twins, the other kidney secreting well. The operative findings were similar and finally, the macroscopic and microscopic pathology were identical.

These facts confirm McFarland's and Meade's conclusions on identical, homologous twins:—"Tumors occurring in identical twins seem always to be similar, symmetrical and simultaneous. The tumor is of the same type and occurs in the same organ far more frequently in the identical than in the non-identical group."

One point would need further clarification if possible. Why a right tumor and a left tumor? Fuss claims that the presence of a tumor affecting the kidneys, one right, one left, in identical twins, may be explained along the principle of the "concordancy of the reflected image." This concordancy of the reflected image has been described in many cases, e.g. identical twins in which one individual was left handed, the other right handed.

Fuss also described identical twins, one having a wart on the right cheek the other on the left.

SUMMARY

Simultaneous tumors in identical twins have been presented. This case is probably the first histologically proven case arising in identical twins. Embryological explanations of the fact that one tumor invaded the right kidney in one twin and the left kidney in the other were offered.

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REFERENCES

Bobbio, L.: Arch. d. mal. des reins, **9:** 571, 1935.
Dean, A. and Pack, G.: J. A. M. A., **98:** 10, 1932.
Deuticke, P.: Deutsche Ztschr. f. Chir., **231:** 767, 1931.
Ewing, J.: Neoplastic Diseases. Philadelphia: W. B. Saunders Co., 1928.
Fister, G. M.: J. Urol., **57:** 488, 1947.
Macklin, M. T.: J. Hered., **13:** 277, 1940.
Ladd, W.: J. A. M. A., **117:** 1858, 1941.
Maslow, L.: J. Urol., **43:** 75, 1940
McFarland, J. and Meade, T. S.: Am. J. Med. Sc., **184:** 66, 1932.
Priestley, J. T. and Broders, A. C.: Proc. Staff Meet., Mayo Clin., **10:** 81, 1935.
Walker, G.: Ann. Surg., **26:** 529, 1879.

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SQUAMOUS CELL CARCINOMA OF THE RENAL PELVIS[1]

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A study of squamous cell carcinoma of the renal pelvis by the combined urological services of the Roswell Park Memorial Institute, and the Buffalo General Hospital, Buffalo, New York was undertaken because of the interesting association of this disease with chronic infection and renal calculi, and its highly malignant nature. Squamous cell carcinoma of the renal pelvis is a relatively rare disease. In 1949, Gahagan and Reed[1] reviewed the literature and reported only 106 cases of which 3 were their own. To this number, we wish to add a review of 15 additional cases.

Four cases with associated renal calculi are presented in detail. The remaining eleven cases are briefly summarized.

CASE REPORTS

Case 1. Mrs. R. H. (BGH No. 206347), a 79 year old white woman was admitted May 27, 1949 complaining of gross hematuria on several occasions since December 1948. She also had severe pain in the right costovertebral angle radiating to the right lower quadrant and right inguinal area. There was no history of weight loss and no passage of stones. In 1932, a large calculus was removed from the right renal pelvis and a right nephropexy was also performed. Since 1932 until the present, the patient had experienced several bouts of pain in the right costovertebral angle with associated chills and fever.

The temperature, pulse and respiration were normal. The blood pressure was 170/96. There was tenderness in the right flank over a well healed right flank incision. No masses were felt. Urinalysis of a catheterized sample revealed the color to be dark red, 3 plus albumin, many pus cells and loaded with red blood cells. A urine culture showed B. coli and enterococci. A complete blood count showed 4,200,000 red blood cells; hemoglobin 11.5 gm.; 5,300 white blood cells; band forms 4; filaments 72; esoinophils 2; basophils 1; lymphocytes 19; monocytes 2. Blood chemistry consisted of a blood glucose of 118 mg. per cent, blood urea of 11 mg. per cent, blood calcium of 9.8 mg. per cent and phosphorus of 2.8 mg. per cent.

Retrograde pyelográms showed complete contraction of the entire upper collecting system and pelvis of the right kidney. At the right ureteropelvic junction, there was noted irregularity with a filling defect, below which the ureter appeared moderately dilated. There was sharp demarcation between the area of defect and the dilated ureter. The collecting system on the left showed some secondary dilation, with blunting of calyces. The kidney shadow appeared approximately normal in size on the right.

Read at annual meeting, Northeastern Section, American Urological Association, Bolton Landing, N. Y., September 14, 1950.

[1] Gahagan, H. Q. and Reed, W. K.: J. Urol., 62: 139, 1949.

Impression: Papillary tumor superimposed upon a chronic contracted right collecting system.

A right nephrectomy was advised, but the patient refused surgery and was discharged June 8, 1949.

The patient was re-admitted August 15, 1949 with persistent hematuria, and pain in the right lower quadrant and right flank.

On August 17, 1949, a right nephrectomy was performed without difficulty. The postoperative course was uneventful and the incision healed well.

Pathologic report: The surface of the kidney was nodular. On section, there was almost complete fibrosis of the kidney parenchyma. There was about 2 cm. of ureter attached and this was thickened. The pelvis was almost obliterated by fibrous tissue.

Microscopic diagnosis: All sections showed, in the fibrotic portions, infiltrating squamous cell carcinoma (fig. 1, *A*).

The patient was discharged from the hospital on September 3, 1949. She expired in November 1949, 3 months following nephrectomy. An autopsy was not obtained.

Case 2. Mr. H. A. (BGH No. 206874), a 77 year old white man was admitted June 9, 1949 complaining of pain in the left flank of 2 months' duration. He also had nausea and emesis. He had lost 20 pounds in weight. He denied hematuria and dysuria. His past history and family history were negative.

The temperature, pulse and respiration were normal. The blood pressure was 156/70. There was a sense of resistance felt in the left upper quadrant with some voluntary muscle spasm in this area. Urinalysis showed a cloudy urine with a trace of albumin and loaded with pus cells and red blood cells. A urine culture revealed B. coli. A complete blood count showed 4,000,000 red blood cells; hemoglobin 10.7 gm.; white blood cells 7,500 with a normal differential. Blood urea was reported as 14 mg. per cent and a blood sugar of 105 mg. per cent was obtained.

A flat film of the abdomen revealed an enlarged left kidney filled with multiple calculi. A complete cystoscopic examination was performed and the examiner reported the bladder urine to be turbid and the presence of a low grade cystitis. A 5F ureteral catheter was passed 25 cm. up the right ureter, and clear urine was obtained. A catheter could not be passed up the left ureter due to an obstruction approximately 3 cm. above the left ureteral orifice; pus was seen to ooze from this left ureteral orifice. Indigo carmine injected intravenously appeared from the right kidney in adequate time with good concentration. No dye appeared from the left.

Impression: Normal right kidney, infected left kidney with multiple calculi.

A left nephrectomy was performed on June 13, 1949 without any difficulty. The postoperative course was uneventful and the incision healed well.

Pathologic report: The surface of the kidney was nodular. Portions of the ureter attached measured 6 cm. On section, the kidney contained a large amount of purulent material, and there was a large staghorn calculus filling out the pelvis. There was no normal kidney parenchyma remaining. The pelvis and calyces were markedly dilated and showed marked inflammation.

Microscopic: Sections through the thickened portions of the kidney shell showed an infiltrating squamous cell carcinoma arising in the pelvis. In other sections, the pelvis showed squamous metaplasia (fig. 1, *B*).

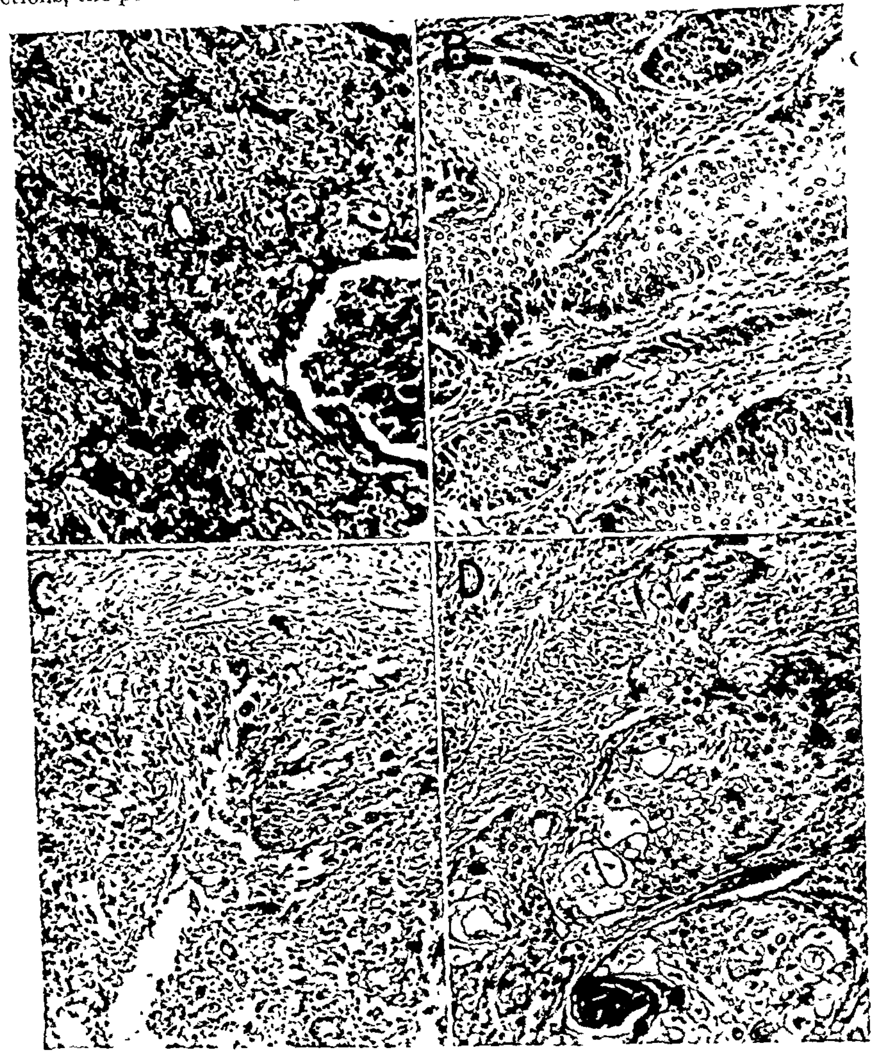

FIG 1 *A*, case 1. Anaplastic squamous cell carcinoma of renal pelvis. Tumor cells are small, anaplastic in type and infiltrating in character.

B, case 2. Squamous cell carcinoma of renal pelvis. Tumor cells are infiltrating in large plaques showing some attempt towards differentiation.

C, case 3 Squamous cell carcinoma of renal pelvis. Tumor cells as a rule show differentiation and degeneration.

D, case 4. Squamous cell carcinoma of renal pelvis. Marked degree of differentiation with keritonization and pearl formation.

The patient was discharged from the hospital on June 22, 1949. He was seen again in December 1949, and complained of severe lumbosacral back pain. An x-ray of the lumbar spine showed a metastatic lesion involving D12 and L1.

In March 1950, x-rays of the ribs showed metastatic involvement. The patient expired April 23, 1950, approximately 10 months following nephrectomy. An autopsy was not obtained.

Case 3. Mr. W. H. P. (BGH No. 347253), a 60 year old white man was admitted on January 9, 1944 complaining of left costovertebral pain radiating down to the left leg. This pain had been intermittently present for 10 years. Since December 22, 1943, the pain had become more acute and constant. During the past 2 months, he had lost 35 pounds. His appetite had been poor for the same length of time and he had had occasional dysuria, but no gross hematuria.

Physical examination revealed a firm, fixed mass in the left upper quadrant. The blood pressure was 120/80.

Cystoscopic examination revealed a low grade cystitis. A catheter was passed up the right ureter and clear urine was obtained. No catheter could be passed up the left ureter. Indigo carmine dye appeared from the right side in 4 minutes, none appeared on the left side in 25 minutes.

The laboratory findings were as follows: Urea nitrogen 13 mg. per cent; CO_2 combining power 46 per cent; serum chlorides 590 mg. per cent. The urine was yellow, cloudy, specific gravity 1.019, neutral, 3 plus albumin, negative glucose, many leukocytes per high power field and squamous renal cells were found; red cells 3,000,000, hemoglobin 7.4 gm.; white blood cells 15,000; 2 juveniles; 29 bands, 47 filaments, 1 eosinophil; 1 basophile; 15 lymphocytes, 5 monocytes.

An excretory urogram showed prompt excretion on the right side. The pyelogram was not unusual in appearance. There was no excretion on the left side. There was apparently a huge kidney on the left, containing multiple stone shadows and areas of parenchymal calcification. The right kidney was not unusual in size, shape or position.

On January 13, 1944, a left nephrectomy was performed. A very large adherent kidney was found quite high. In separating the pelvis, it was opened and approximately one pint of pus escaped. Culture of this pus revealed an anaerobic streptococcus.

The pathologic report revealed a kidney partly with torn cortex in a semicollapsed state, measuring 15 by 9 cm. in width and 7 cm. in thickness. On section, all calyces were maximally distended and filled with slightly bloody tinged, fairly fluid exudate of greyish-red color. In several distended calyces were combination stones, some of which formed typical casts of the calyx. Near the central portion and extending into the entire calyces of the lower pole, there was a diffuse greyish-red growth covering the mucosa of the calyx and the pelvis, and infiltrating the remainder of the cortex in this part of the kidney. The thickness of the hydronephrotic sac varied between 1 and 3 cm. There was a large number of smaller concrements embedded into the previously mentioned exudate within the recesses of the calyces. Microscopic findings: Mature squamous cell carcinoma with considerable keratinization, distinct infiltrative tendencies but of very high differentiation, with hardly any evidence of anaplastic cells, were found. Considerable necrosis and necrobiosis were present in the keratinized material. Unusually marked inflammatory infiltration was noted throughout the parenchyma of the kidney. The mucosa of the many calyces around the center of the tumor was entirely replaced by the same squamous cell proliferating growth.

The perihilar tissue and in part a great deal of the cortical parenchyma showed almost complete hyalinized fibrosis.

Diagnosis: 1) Squamous cell carcinoma of renal pelvis (fig. 1, *C*); 2) extensive ascending infection. The patient made an uneventful recovery following surgery and was discharged on January 26, 1944. He gradually went downhill at home and died of generalized carcinomatoses on May 20, 1944, five months following nephrectomy.

Case 4. Mrs. A. R. (BGH No. 178365), a 53 year old white woman, was admitted to the Buffalo General Hospital on October 14, 1945. Since May 1944, she had lost 10 pounds in weight, felt tired and gave the history of hematuria, one time. She stated that she had first noted hematuria in 1942. She had no other urological complaints.

Physical examination was essentially normal except for a large palpable tender left kidney. The blood pressure was 160/105.

Urinalysis revealed yellow clear urine with 1.017 specific gravity. Reaction was acid. It was negative for albumin and glucose. Microscopic examination revealed 1–3 white blood cells per high power field; red blood cells 4,220,000 with 82 per cent hemoglobin. The white blood cells numbered 14,700 with 15 bands, 65 filaments, 1 eosinophil, 15 lymphocytes and 4 monocytes.

The Wassermann test was negative. Glucose was 149 mg. per cent, urea nitrogen 14 mg. per cent and chlorides 575 mg. per cent. Excretory urography revealed a nonfunctioning left kidney with 5 calculi in the renal pelvis and calyces.

On October 17, 1945, a left nephrectomy was performed.

The kidney measured 14.5 by 7 by 5 cm. and weighed 1200 gm. On section, there was marked chronic pyonephrosis, with, for the most part, extreme pyonephrotic atrophy of the parenchyma and with a few fragments of calculi within the dilated calyces.

The kidney pelvis and calyces were filled with distinctly cloudy urine.

Microscopic examination revealed an apparently uniformly diffuse malignant metamorphosis of the epithelium of the calyces into a keratinizing squamous cell carcinoma in some areas (fig. 1, *D*), with very massive and deep infiltration into the kidney parenchyma. The tumor itself was tremendously inflamed and in some areas, showed extreme hyperkeratosis of the surface layers.

The remainder of the parenchyma showed very marked signs of chronic pyelonephritis with hyalinization of almost all glomeruli, considerable interstitial fibrosis and marked thickening of small arteries. Also, many reactive lymph follicle formations were noted.

The patient made an uneventful recovery following surgery and was discharged on October 31, 1945. High power x-ray therapy was begun, but had to be discontinued after 4 treatments of 100 r each. She remained in good condition until April 15, 1946 when she began to go downhill and died on August 8, 1946 at home. No autopsy was performed.

Case 5. Mr. A. N. C. (RPMI No. 37086), a 43 year old white man, had symptoms of weight loss, pyuria, weakness and anorexia of 1 year's duration. A left nephrectomy was performed. The pathological report was squamous cell carcinoma of the renal pelvis. The patient expired 4 months following nephrectomy.

Case 6. Mrs. S. W. (RPMI No. 8783), a 47 year old white woman had symptoms of hematuria, pyruia, loss of weight and pain of 1 month's duration. A right nephrectomy was performed. The pathologic report was squamous cell carcinoma of the renal pelvis. High power x-ray was begun postoperatively but had to be discontinued, because the patient could not tolerate it. The patient expired 4 months following nephrectomy.

Case 7. Mr. F. R. (RPMI No. 12082), a 48 year old white man, had symptoms of hematuria, right flank pain and weight loss of 6 months' duration. A right nephrectomy was performed. The pathologic report was squamous cell carcinoma of the renal pelvis. High power x-ray therapy was given and patient received a full course. This patient also had a papillary carcinoma of the urinary bladder, which was diagnosed and treated 13 months following the nephrectomy. The patient expired 23 months following nephrectomy.

Case 8. Mrs. F. M. (RPMI No. 52461), a 53 year old white woman, had symptoms of pain in the right flank, loss of weight and pyuria of 9 months' duration. A right nephrectomy was performed. The pathologic report was squamous cell carcinoma of the renal pelvis. The patient expired 10 months following nephrectomy.

Case 9. Mr. A. S. (RPMI No. 56301), a 73 year old white man with symptoms of severe back pain, pyuria, loss of weight and anorexia of 18 months' duration. A right nephrectomy was performed. The pathologic report was squamous cell carcinoma of the renal pelvis. High power x-ray therapy was begun postoperatively but had to be discontinued because the patient could not tolerate it. The patient expired 9 months following nephrectomy.

Case 10. Mr. S. C. (RPMI No. 41690), a 52 year old white man had symptoms of hematuria, pain in the right flank and loss of weight of 6 months' duration. A right nephrectomy was performed. The pathologic report was squamous cell carcinoma of the renal pelvis. High power x-ray therapy was begun but had to be discontinued because the patient was unable to tolerate it. The patient expired 6 months following nephrectomy.

Case 11. Mrs. C. M. RPMI No. 46953), a 67 year old white woman, had symptoms of pain in the left flank, pyuria, loss of weight and anorexia of 3 years' duration. A left nephrectomy was performed. The pathologic report was squamous cell carcinoma of the renal pelvis. High power x-ray therapy was given postoperatively and the patient received the entire series of treatment. The patient expired 15 months following nephrectomy.

Case 12. Mrs. B. H. (RPMI (No. 24234), a 61 year old white woman, had symptoms of severe pain in the left flank, pyuria and loss of weight of 8 months' duration. A left nephrectomy was performed. The pathologic report was squamous cell carcinoma of the renal pelvis. This patient also had a carcinoma of the cervix, which was treated with interstitial radiation and surgery 2 years prior to nephrectomy. High power x-ray therapy was begun, but patient expired before a full course was completed. Death occurred 2 months following nephrectomy.

Case 13. Mrs. K. L. (BGH No. 132707), an 81 year old white woman had symptoms of pain, pyuria, weight loss and a mass in the epigastrium. An exploratory laparotomy was performed with biopsy. The patient expired within 24 hours following surgery and an autopsy revealed a squamous cell carcinoma of the right renal pelvis with extensive metastatic disease.

Case 14. Mrs. J. S. (BGH No. 121759), a 64 year old white woman, had symptoms of hematuria, pyuria, right flank pain and a palpable mass. A right nephrectomy was performed. The pathologic report was squamous cell carcinoma of the renal pelvis. The patient expired 6 months following nephrectomy.

Case 15. Mrs. H. G. (BGH No. 119650), a 72 year old white woman had symptoms of hematuria, pain, pyuria and mass in the left upper quadrant. A left nephrectomy was performed. The pathologic report was squamous cell carcinoma of the renal pelvis. The patient expired 45 months following nephrectomy.

INCIDENCE

Primary tumors of the renal pelvis have been reported by various authors[2, 3] as occurring between 5 and 15 per cent of all renal neoplasms. Of this percentage, squamous cell carcinoma constituted only 17 per cent of the pelvic tumors.[4] The sex incidence is almost equal. In our series, there were 9 females and 6 males. The youngest individual in this series of 15 cases was 43 years of age and the oldest 81, with an average age incidence of 62. There was little difference in the side involved. Eight lesions were found in the right kidney pelvis and seven in the left.

ETIOLOGY

This disease is nearly always associated with long standing chronic infection. Another interesting feature is the fairly high percentage of associated renal calculi. The presence of infection with resultant irritation over a prolonged period of time has been considered by many to be one of the causes of metaplasia of normal tissue into a malignant growth. Whether or not this theory holds true is difficult to say, yet, one must note that the presence of infection in such a large percentage of cases is more than coincidental. Renal calculi in the presence of squamous cell carcinoma of the renal pelvis has been reported by many authors as varying between 25 per cent and 60 per cent. Gahagan and Reed reported the incidence of renal calculi in 48 of 106 cases. Gilbert and MacMillan[5] in their series reported that 30 of 57 cases or 52 per cent were associated with stones. Martin and Mertz[6] concluded in their review that the calculus was primary and the tumor was secondary in 14 or 63 per cent of 22 cases of epithelial tumors of the pelvis and ureters. In our series of 15 cases, there were four or a 26 per cent incidence of associated renal stones.

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[2] Harvey, N. A.: J. Urol., **57**: 669, 1947.
[3] Melen, D. R.: J. Urol., **51**: 386, 1944.
[4] Kutzmann, A. A.: J. Urol., **39**: 487, 1938.
[5] Gilbert, J. B. and MacMillan, S. F.: Ann. Surg., **100**: 429, 1934.
[6] Martin, H. H. and Mertz, H. O.: Mississippi Valley Med. J., **24**: 74, 1917.

Early nephrectomy is the treatment of choice. Radiation is poorly tolerated and of doubtful value.

Prophylaxis should include removal of calculi, vigorous treatment of chronic infection and removal of seriously damaged kidneys.

The prognosis is poor and probably will continue to be so because of the late diagnosis and infiltrative character of the lesion.

SUMMARY

A brief outline of the incidence, etiology, pathology, symptomatology, diagnosis and treatment of squamous carcinoma of the renal pelvis is presented.

Four cases with associated renal calculi are reported in detail.

Eleven additional cases are summarized.

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URETERAL IMPLANTATION OF RENAL ADENOCARCINOMA

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The occurrence of implants in the ureter arising from adenocarcinoma of the renal parenchyma is rare. MacAlpine[1] reported such an instance in 1948 and in searching the literature collected 12 cases. A review of the literature since the publication of MacAlpine's article has resulted in an additional case reported by Hovenanian in 1950.[2]

The mechanism of implant or re-seeding is the same for viable tumor cells whether they originate in the tubular or pelvic portion of the kidney. Careful cytological study of urine from all types of renal neoplasms reveal both viable and desquamated tumor cells. Hovenanian[2] believes the reason why more renal adenocarcinoma seedlings have not resulted lies in the type of epithelium involved. This theory is reasonable if one considers the entirely different environment of cells arising from the renal tubules in contrast to those arising from transitional mucosa. Such an explanation is justified by the relative common occurrence of implants associated with papillary carcinoma of the renal pelvis in contrast with the rarity of implants arising from parenchymal carcinoma.

The site of implants in the cases reported includes all levels of the ureter. Multiple implants have occurred in several instances. Implantation is not limited to the ureter as evidenced by a case reported by Sżymonowiez[3] in 1932 describing an implant in the urethra. The time interval between nephrectomy and clinical evidence of implant varied from 1 month to 5 years.

The following case is presented to illustrate the presence of secondary implantation of renal adenocarcinoma and failure to recognize such an implant prior to nephrectomy.

CASE REPORT

D. N. B., No. 16815, a 44 year old executive engineer, was admitted to Methodist Hospital September 20, 1949, because of gross, intermittent, silent hematuria of 1 week's duration. He had noted some vague distress in the right upper abdomen for 3 weeks. A few hours prior to admission some colic in the right abdomen was followed by the passage of blood clots in the urine. He had had no weight loss, fever or cough. Past history and family history were not significant.

The general physical examination revealed a well nourished and well developed patient. Abnormal findings consisted of a palpable movable nontender mass in the right kidney area.

The urine was alkaline in reaction, specific gravity, 1.030, albumin O, sugar 0; microscopic examination revealed an occasional white blood cell and many red blood cells.

Read at annual meeting, North Central Section, American Urological Association, Milwaukee, Wis., October 12, 1950.

[1] MacAlpine, J. B.: Brit. J. Surg., 34: 164–168, 1948.

[2] Hovenanian, M. S.: J. Urol., 64: 188–192, 1950.

[3] Symonowiez, J.· Cited by MacAlpine.

Hemoglobin 13.5 gm. (88 per cent), red blood cells, 4,490,000, white blood cells, 9,700 with a normal differential count, nonprotein nitrogen, 41 mg. per cent.

X-ray examination of the chest was essentially negative except for some accentuation of the basal bronchovascular markings on the right.

Cystoscopic examination disclosed a normal bladder except for bloody urine spurting from the right ureteral orifice. A small filament of grayish white tissue interpreted as old blood clot was seen protruding from the right ureteral orifice. Ureteral catheters were passed to both kidney pelves without difficulty. Examination of the left ureteral specimen of urine was normal. The right ureteral specimen was loaded with red blood cells.

A plain x-ray showed a normal left renal shadow. The shadow of the right kidney was enlarged. The osseous structures were normal. The left pyelogram was normal. The right pyelogram revealed extrinsic pressure on an elongated renal pelvis with obliteration of the middle calyces and blunting of the upper and lower calyces.

A preoperative diagnosis of tumor of the right kidney was established. On September 23 a right nephrectomy was performed through a loin incision. The midportion of the kidney was nodular with extension of tumor into the renal pedicle resulting in considerable difficulty in ligation of the renal pedicle.

Gross examination of the specimen revealed a large tumor mass of yellowish gray color showing central hemorrhagic degeneration. The pelvis and renal vein were invaded by tumor by direct extension and penetration.

Microscopic sections examined by Dr. H. M. Banks, pathologist, demonstrated proliferation of dark staining neoplastic cells of large size arranged in a pseudoglandular structure and showing numerous mitotic figures. The diagnosis was adenocarcinoma of the kidney (fig. 1, *A*).

The postoperative course was uneventful with good wound healing and discharge from the hospital October 3, 1949, on the tenth postoperative day.

The patient received x-ray therapy over his anterior lateral and posterior right kidney areas during the period of October 13 to November 10. Each field received 2100 r. On October 31 examination of the urine revealed 1 plus albumin and a few red blood cells.

The patient was re-admitted to Methodist Hospital on November 14, 1949 because he had experienced dysuria, urgency, and frequency followed by gross hematuria and the passage of blood clots. He also complained of some pain over the right sacral area.

The nephrectomy scar was well healed and no induration was noted in the wound.

The urine was loaded with red blood cells. The nonprotein nitrogen 30 mg. per cent, hemoglobin 12 gm. (78 per cent), red blood cells 3,490,000, white blood count, 8,250.

Cystoscopic examination on November 14, 1949 revealed a freely bleeding tumor resembling a raspberry 1 cm. in diameter extending from the right ureteral orifice. No other evidence of tumor was seen. A biopsy was obtained following which an electrode was introduced into the intramural portion of the right ureteral orifice and the area electrocoagulated. Following this procedure there was no further bleeding.

Microscopic examination of the tissue as reported by Dr. H. M. Banks, pathologist, showed a loose stroma, with numerous cells of large size and dark staining characteristics and evidence of neoplastic variation and numerous mitotic figures. In some areas there was a mosaic pattern with the cells showing a dark staining nucleus and large vacuolated periphery. Diagnosis: neoplasm morphologically resembling adenocarcinoma of kidney (fig. 1, *B*).

X-ray study on October 17 failed to reveal any evidence of metastases.

On November 18 a right ureterectomy was performed through a modified hockey stick incision. No gross evidence of tumor was found in the peri-ureteral tissue. The bladder was opened to permit adequate excision of a cuff of bladder about the intramural ureter and the ureteral orifice. The bladder was closed about a suprapubic drainage tube.

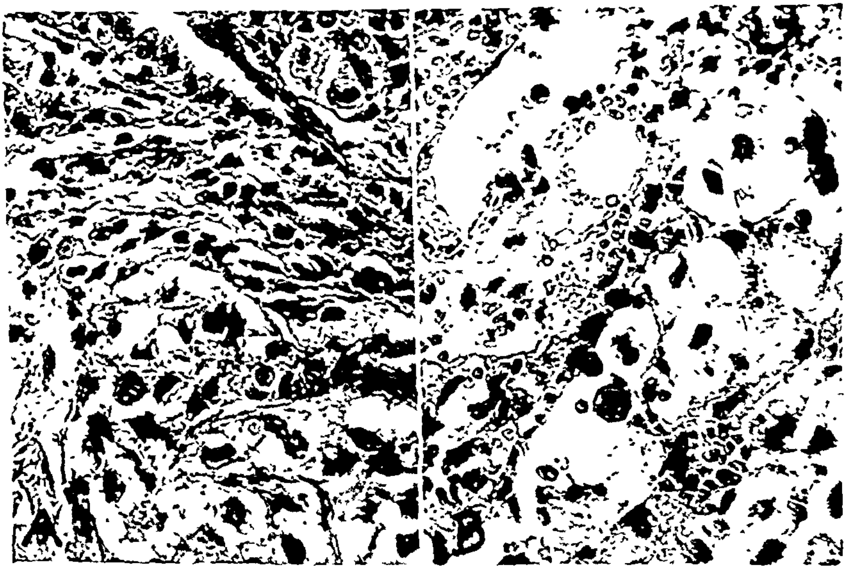

FIG. 1. A, Section of kidney tumor, × 240. B, implant in right ureter, × 240.

The ureter measured 13.9 cm. in length. A tumor mass measuring 1.5 cm. in diameter occupied the distal portion of the intramural ureter. Microscopic study by Dr. H. M. Banks, pathologist, demonstrated the entire proximal ureter to be normal. The intramural ureter showed a transitional epithelium of benign appearance except in one area where there was a mass of dark staining cells of large size resembling adenocarcinoma of the kidney.

The postoperative course was complicated by wound infection and pyelonephritis. About a week following surgery the patient developed a persistent headache and some disturbance in vision. The right pupil was noted to be constricted. The patient was discharged from the hospital December 7, 1949.

Following discharge from the hospital there was a gradual development of pain radiating down the left arm. On December 13 a smooth, hard, fixed mass measuring 4 by 2 cm. was noted in the left supraclavicular region. X-ray study of the chest showed nodules of increased density throughout the right lung and a density beneath the left clavicle. The supraclavicular gland continued to increase in size despite x-ray therapy to a total 2192 r.

The patient continued to run a downhill course with increasing headache, blurring of vision, dysuria and discomfort terminating in coma with death January 18, 1950. Postmortem examination was not obtained.

DISCUSSION

The incidence of implants secondary to renal adenocarcinoma is probably higher than is indicated by reports in the literature. Hovenanian[2] suggests that the trauma incident to manipulation of the kidney during nephrectomy may be a major factor in the reported cases. Such was not the status of the case presented.

In retrospect it seems very obvious that a gross error was accomplished in mistaking a filament of implant in the ureteral orifice for what seemed to be a fragment of dislodged blood clot.

SUMMARY

The incidence of implantation secondary to parenchymal renal adenocarcinoma suggests the necessity for thorough search for such implants in the ureter and bladder and urethra both in the preoperative investigation preparatory to nephrectomy and in the postoperative follow-up period.

Hematuria following nephrectomy for renal parenchymal adenocarcinoma suggests the presence of an implant.

Implantation may occur in the absence of surgical manipulation.

A case of ureteral implantation of renal adenocarcinoma is reported.

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AN EVALUATION OF URETEROSIGMOID ANASTOMOSIS BY MUCOSA-TO-MUCOSA METHOD AFTER TWO AND ONE-HALF YEARS' EXPERIENCE

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Two and a half years' experience with ureterosigmoid anastomosis by the mucosa-to-mucosa method has brought forth a number of interesting findings. We are well aware of the fact that the interval is too short to evaluate the results of cancer surgery, but we believe that certain conclusions can be drawn concerning late results of ureterosigmoid anastomosis. In addition, we should like to present certain difficulties that have arisen as these cases have been followed through the years.

The following problems will be discussed: 1) immediate and late mortality and morbidity; 2) urinary sepsis; 3) air pyelograms and ureteral reflux; 4) early and late excretory urography; 5) acidosis and hyperchloremia.

Included in this series are cases from the private service of Dr. D. K. Rose and myself, and those done by the Resident Staff of the U. S. Veterans Hospital, Jefferson Barracks, Missouri and Barnes Hospital, St. Louis, Missouri. We concur completely with the opinion expressed by many others that the operation of ureterosigmoid anastomosis is one that should not be undertaken lightly, as attested by the fact that it was performed for nonmalignant disease in only 3 of our series of 54 cases. Each of these 3 were hopeless urological cripples prior to the transplants.

IMMEDIATE AND LATE MORTALITY AND MORBIDITY

A total of 54 successive cases have been done by this method without a single postoperative mortality, all patients having been discharged from the hospital under their own power.

The average age was 61, the youngest operated on for malignant disease, 38, and the oldest 78. Forty patients had bilateral ureterosigmoid anastomosis and cystectomy in one stage. Five had two-stage procedures, and in 9 cases, ureterosigmoid anastomosis alone was done. It is our belief that the cystectomy is much easier to perform at the time of ureterosigmoid anastomosis, and that the added surgery does not increase the operative risk any more than a second stage cystectomy would do.

Immediate postoperative complications have been relatively uncommon. There were 4 postoperative eviscerations and 3 incisional hernias. We believe these were in part due to the modified Cherney incision which was used on all the earlier cases. Since changing to a midline incision, this complication has not occurred. Two cases had troublesome ileus for several days. There was one retropubic abscess and one case of acidosis. Three patients developed fecal

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fistulas. However, each of these was due to rectal involvement by carcinoma or surgical trauma and had no apparent connection with the anastomosis.

The late results are shown in table 1. Of the total of 54 patients, 33, or 61 per cent, are still living. It is notable that in the 2–2½ year group over 50 per cent are still alive. Of the 8 living, 3 were operated upon for nonmalignant disease. Of these 8, all are carrying on normal activities and appear to be in reasonably good health. Although 39 per cent of the patients operated upon are dead, we wish to emphasize that no patient has been refused surgery whom we felt could stand the operative procedure. A great many patients with advanced carcinomas, for whom little hope for cure was held, have been operated upon with the belief that the palliation obtained was worth the surgery involved. In our experience this belief has been well substantiated.

The average length of survival of those patients who have expired was 11.1 months, the shortest period of survival being 2 months, and the longest 20 months. Of the patients who have expired, 3 have died from causes directly referable to the ureterosigmoid anastomosis. Two others died rather suddenly of unknown causes, and it is quite possible that their death was due to unrecognized acidosis and therefore they should be included as having been due to the operation. One patient who expired after 20 months died of acidosis, which was recognized too late, and improperly treated. At autopsy, there was no evidence of recurrence of the carcinoma. Therefore, about 15 per cent of the total deaths may be directly attributed to the ureterosigmoid anastomosis. The balance died of advanced carcinomatosis or complications therefrom.

TABLE 1

YEARS	ALIVE	DEAD
0–½	5	1
½–1	9	3
1–1½	7	3
1½–2	4	7
2–2½	8	7
Total	33	21

URINARY SEPSIS

Since all patients were placed on antibiotics during the immediate postoperative period, early sepsis presented a problem in only one case and disappeared after about two days of rectal drainage. None of the other cases presented any evidence of urinary sepsis in the immediate postoperative period.

Of a total of 48 cases in which an accurate follow-up was obtained, 27, or 56 per cent, have had no chills, fever, or other evidence of urinary sepsis. Twelve had a minimal amount of chills and fever. In this category we considered those who had had two or less episodes of sepsis. Seven were considered to have had moderate urinary sepsis and two are listed as severe. In one of the latter, kidney infection was undoubtedly the primary cause of death, although acidosis may have played a part. In the other, the patient had marked hypertension preoperatively, and had an aneurysm of the abdominal aorta. However, he did experience considerable urinary sepsis and therefore it was felt that in all fairness we must consider it as a contributory factor in his death.

In general, I believe that we can state that urinary sepsis has not presented any great problem in these cases. Each episode of infection has, with one exception, been readily controlled by the usual antibiotics or chemotherapy, and has been of relatively short duration. In addition, we have observed that as the patient continues postoperatively, there is apparently some degree of natural immunity built up to the intestinal organisms. In several patients, we have observed a decreasing severity both in the character and frequency of the attacks.

AIR PYELOGRAMS AND URETERAL REFLUX

The presence of air pyelograms following direct anastomosis has been mentioned as an objection to this method. In our experience, this has not been the case. All postoperative pyelograms up to as long as 2 years postoperatively were reviewed for air pyelograms. Air was found to be present in the kidney pelvis in only 5 kidneys from the entire series. With one exception, these were present in kidneys which were nonfunctioning preoperatively. It is interesting to note that these patients had very few symptoms and sepsis was not a pronounced problem in any of them. If one transplants a hydronephrotic ureter, with marked fibrosis in the musculature, and poor peristalsis, it is inevitable that postoperative difficulties will develop.

TABLE 2. *Forty-seven patients with accurate pyelograms and follow-up*

	PREOPERATIVELY	POSTOPERATIVELY
No. of kidneys studied	92	91
Normal	62	41
Hydronephrosis	18	31
Nonfunctioning	9	7
Decreased function	3	12

A total of 16 patients were studied for reflux, the study being made by filling the colon with a skiodan enema under considerable pressure, and then taking a flat film. This study included only 31 kidneys, one patient having had a nephrectomy prior to ureterosigmoid anastomosis. Of the 31 kidneys, 5 showed a reflux of skiodan up the ureters. In only one patient was the reflux bilateral.

EARLY AND LATE EXCRETORY UROGRAPHY

The total number of patients with accurate pyelograms and follow-ups was 47. For the purposes of more accurate evaluation, the data are broken down into the total number of kidneys. A preoperative and postoperative comparison is incorporated in table 2.

A number of the postoperative hydronephroses so listed were very minimal in character. Many patients who showed a mild dilatation immediately postoperative had a definite reduction in dilatation on films taken at a later date.

It is noteworthy that two kidneys which were listed as nonfunctioning on excretory urography preoperatively regained some function postoperatively. However, the number of normal kidneys was reduced from 62 to 41, or a decrease of approximately 34 per cent. Likewise decreased function was noted in 12 kidneys. In most instances these showed poor dye shadow, but as far as could be determined, no actual hydronephrosis existed. Although many factors contribute to faint shadows in excretory urography, we consider these results as unfavorable. Repeated pyelograms were made on many of these patients, some for as long as two years postoperatively. In only one case did we note progression of the hydronephrosis. Surprisingly enough, this patient has no urinary sepsis and is maintaining a normal nonprotein nitrogen.

ACIDOSIS AND HYPERCHLOREMIA

One of the major problems in caring for the patient with ureterosigmoid anastomosis is that of acidosis. Very early in our experience we encountered an extremely interesting case, which emphasized this problem, but it was not until subsequent cases of acidosis began to appear that we realized its true significance. This first patient was a 54 year old Negro, who was admitted to the Veteran's Hospital with extensive carcinoma of the bladder, and involvement of both ureteral orifices to such an extent that excretory urography revealed a completely nonfunctioning kidney on the left, and only slight function with marked hydronephrosis on the right. Urea nitrogen on admission was 42, and he appeared to be in a very serious condition. It was concluded that surgery should be done in two stages. The ureter of the functioning kidney was transplanted to the sigmoid, and 10 days later the second ureter was transplanted and the cystectomy done. The patient had a fairly stormy postoperative course but made a comparatively good recovery, only to return to the hospital about three weeks after discharge with a nonprotein nitrogen of 155 and a carbon dioxide level of 12. He was practically comatose at that time, and required a great deal of intravenous molar lactate to correct his chemical deficiencies. However, he responded surprisingly well to treatment and was discharged on sodium bicarbonate by mouth. Since that time, he has had several hospital readmissions, and each time he was found to have a moderately severe acidosis. However, his general condition has remained good and he is continuing to work at his occupation of cleaning out box cars for a cement company some two years postoperatively. He looks and feels well. This patient stimulated us to make further studies on those patients with ureterosigmoid anastomosis, and we have endeavored to follow as many as possible from this standpoint.

Clinical symptoms which we have encountered have been general malaise, poor appetite, mild nausea, and weakness.

Accurate chemical studies have been obtained on 21 patients. Sodium and potassium levels were normal in the 13 cases in which these determinations were made. Practically all patients showed a moderate elevation of blood chlorides whether acidosis or elevated blood nonprotein nitrogen was present or not. Of the 21 cases studied, 33 per cent had carbon dioxide values of 50 volumes per cent or above (these were considered to be normal); 24 per cent had a carbon dioxide level of 40–48 volumes per cent: and 43 per cent had carbon dioxide levels below 40 volumes per cent. All but two of these were between 30–40 volumes per cent. It is noteworthy that an elevation of blood nonprotein nitrogen occurred in only those patients who had advanced kidney damage and were listed as having expired from kidney disease. In none of the others was there any appreciable elevation of the nonprotein nitrogen, either early or late. There seemed to be no relation between the carbon dioxide level and the blood nonprotein nitrogen. This point emphasized the fact that a simple determination of nonprotein nitrogen is not sufficient to evaluate the condition of a patient who has had a ureterosigmoid anastomosis. We believe that our incidence of acidosis is no higher than that reported by other methods.

Eleven of these patients were placed on rectal drainage for a five day period, but this seemed to have no appreciable effect on the carbon dioxide levels.

All patients showed a definite elevation of carbon dioxide after the administration of sodium bicarbonate in doses of one teaspoonful four times daily, and in all but four, the carbon dioxide level returned to normal and was maintained there as long as the patient received the bicarbonate. Other measures for the control of acidosis consisted of instructing the patient to empty the bowel at two hour intervals during the day, and limiting the salt intake to that used in cooking.

We concur with the opinion of Ferris and Odel.[1] that the lowered carbon dioxide is in part due to the hyperchloremia following absorption of chlorides from the large bowel. However, one rather interesting fact has appeared in analyzing our cases, and that is that rarely did the lowered carbon dioxide occur early. In most cases it became evident between 4 and 6 months after operation. In our opinion there is a combination of two contributory factors. First, there is inevitably a certain amount of parenchymal renal damage which occurs after ureterosigmoid anastomosis by whatever method used. This damage is probably of sufficient degree that the kidney is no longer able to compensate for the hyperchloremia which is present in all cases. If this renal damage is minimal, then, although the reabsorption of chlorides occurs, compensation takes place, and the patient does not develop acidosis.

Following our experience in observing patients in whom cecal pouches have been made, and in whom acidosis did not appear, we have felt that it might be of value to establish a permanent colostomy, closing the colon just proximal to the sites of the anastomosis and forming an artificial bladder from the rectum. Recently, this procedure was carried out on one patient, and to date his chemical studies have remained satisfactory. We expect to do this operation on several patients to see if the improvement is sufficient to warrant the inconvenience of a permanent colostomy. It is fully realized that this is not a new procedure, but we believe that it might be well worth reconsideration, particularly if the incidence of sepsis and acidosis can be appreciably reduced.

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[1] Ferris, D. O., and Odel, H. M.: Electrolyte pattern of the blood after bilateral ureterosigmoid anastomosis. J. A. M. A., 142: 634–641, 1950.

SUMMARY

An evaluation of early and late results of ureterosigmoid anastomosis done by the mucosa-to-mucosa method has been presented.

A total of 54 cases have been done without a single operative mortality.

Fifteen patients were operated on from 2 to 2½ years ago, and of these, 8, or over 50 per cent, are still alive, carrying out normal activities, and are in comparatively good health.

Urinary sepsis was present in varying severity in 44 per cent of the cases. However, in only two of these were there severe symptoms. The number of cases developing air pyelograms and showing ureteral reflux was minimal, occurring in most instances in kidneys which were nonfunctioning preoperatively.

Early and late postoperative excretory urography compares favorably with reports on excretory urograms where other methods were used.

The late development of acidosis in patients who have had ureterosigmoid anastomosis is a very real and important problem, but is well controlled when recognized. The establishment of a rectal pouch with a permanent colostomy may eventually prove to be the solution for this problem.

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STRANGULATED INTERNAL HERNIA AS A COMPLICATION OF URETERO-INTESTINAL ANASTOMOSIS

T. H. SWEETSER

The incident which focused my interest on this subject nearly ended disastrously. My earlier experience and training in general surgery should have kept me out of trouble, but it was that earlier training that led me to recognize the need for prompt surgical relief. It was consoling to find, in discussing the matter orally recently and tonight at dinner, that several of my eminent colleagues have had similar trying experiences, but I have failed to find any such reports in the recent numerous articles on uretero-intestinal anastomosis, or any description of appropriate prophylaxis.

My patient, a 66 year old farmer, had had intermittent hematuria for about 10 months before consulting his doctor. Excretory urograms demonstrated an extensive filling defect of the left half of his bladder. Cystoscopy and biopsies proved a widespread papillary carcinoma, grade 2, with extension to and into the bladder outlet. After the usual preparation, abdominal exploration showed no extensions or metastases. Therefore the ureters were anastomosed to the sigmoid, and the bladder, prostate and vesicles were removed at the time of the exploration. We used the technique of anastomosis described by Reed Nesbit.[1] Implantations were well up in the sigmoid as described in most recent reports. It has seemed to me, since the discussions by Flocks[2], that the blood supply of the ureters is less likely to be inadequate near the pelvic brim than lower down. The patient made an excellent recovery and went home in good condition 14 days after the cystectomy.

Six days later he suffered severe low abdominal pain with nausea but without vomiting or intermittent cramps or borborygmi. A mass could be felt suprapubically. Abdominal exploration done promptly on his return to the hospital discovered free serosanguinous fluid in the peritoneal cavity and a loop of small intestine three and a half feet long in the pelvis, about 3 feet of it being gangrenous. The aperture through which the loop had passed was about 3 cm. in diameter, behind the sigmoid and between the mesosigmoid and the site of implantation of the right ureter into the sigmoid. In reducing the hernia, with much difficulty, I caused a small leak at the anastomosis, but was able to repair it satisfactorily. The strangulated loop was resected by the method of Dennis.[3] The hernial aperture was closed with two rows of fine catgut sutures between the posterior parietal peritoneum and the peritoneum of the mesosigmoid, avoiding the blood vessels. Aureomycin solution was injected high in the left lateral peritoneal gutter before completing closure of the abdomen. The patient made an entirely uneventful recovery and went home again on the fourteenth day after operation.

Read at meeting of the Chicago Urological Society, April 27, 1950.

[1] Nesbit, R. M.: J. Urol., **61**: 728, 1949.

[2] Flocks, R. H.: J. Urol., **59**: 21, 1948.

[3] Dennis, C.: Surgery, **5**: 548, 1939; and Surg. Gynec. & Obst., **77**: 225, 1943.

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[3] Dennis, C.: Surgery, 5: 548, 1939; and Surg. Gynec. & Obst., 77: 225, 1943.

A few instances of intestinal obstruction after uretero-intestinal anastomosis have been reported[4, 5, 6, 7], but this particular source of the trouble was not found, or at least not recognized in the reported cases, and I find no description of appropriate prophylactic measures in the various reported operative techniques.

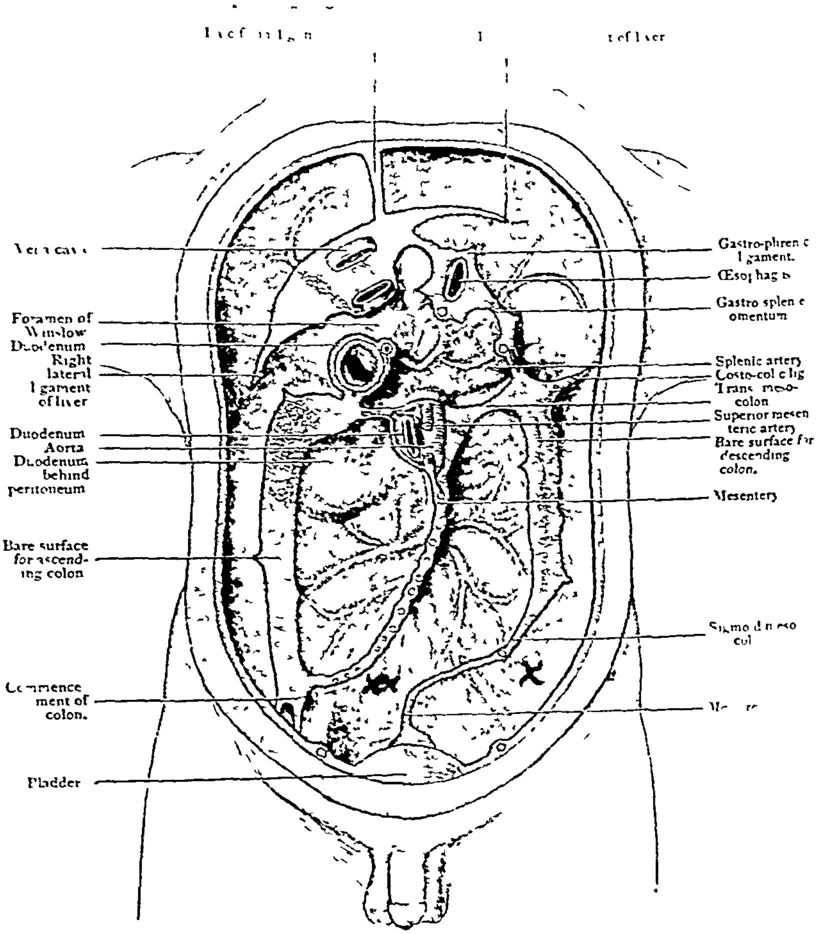

FIG 1 Diagram to show lines along which peritoneum leaves wall of abdomen to invest viscera (Cunningham) (From Morris, H Human Anatomy Philadelphia P Blakiston & Co , 1893, p 1015)

Within the last few years many descriptions have been written of techniques for and results of uretero-intestinal anastomosis Few reports have been made of intestinal obstruction following such operations and none that come within the field of this report, unless the true cause of difficulty in some of these cases was unrecognized In one case, there was obstruction of the rectum by carcinomatous

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[4] Hepler, A B J Urol , 44: 794, 1940
[5] Schmittman, M N Y State J Med , 48: 882, 1948
[6] Marshall, V F J Urol , 58: 244, 1947
[7] Strom, G W Personal communication

tissue filling the pelvis after cystectomy. In one case reported to me orally by Dr. Gordon Strom[7] (a Veterans' Hospital case), there was obstruction by a pelvic abscess due to perforation of the rectosigmoid after cystectomy. Hepler[4] reported 1 case (patient died from fecal fistula 3 years later). Two cases reported were due to adhesions between the sigmoid and posterior peritoneum. One case was reported by V. F. Marshall[6] as small intestinal obstruction at the site of the operation, but no cause was given. Schnittman[5] reported 1 case (may have been the same case). Cordonnier[8] reported that he does not extraperitonealize the sites of implantation for fear of intestinal obstruction, but the inference is that the obstruction would be due to kinking at those points.*

Charles Mayo and Dixon,[9] recognizing the possibility of intestinal obstruction after colostomy, advised in 1927 that the peritoneal pocket or opening (fig. 1, X[10]) between the sigmoid mesentery and the left lateral abdominal wall be obliterated by means of a pursestring suture to avoid the danger of herniation of a loop of small intestine into this space with subsequent obstruction. In figure 1, the hernial aperture artificially produced in our patient is indicated by XX and was closed in a similar manner.

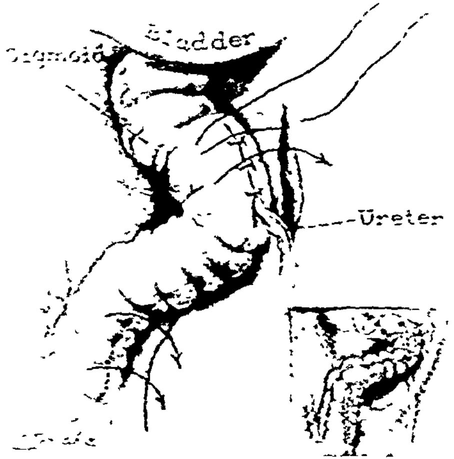

FIG. 2. Bilateral transperitoneal ureterosigmoidostomy. Both anastomoses are through right longitudinal band of colon. (From Ferris and Priestley: J. Urol., 60: 98, 1948.)

The original description of Coffey[11] and those of Schinagel[12] and some others depict the implantations as being made into the rectosigmoid or rectum, where the bowel is in the midline and has no mesosigmoid or very little. In such procedures there would be no chance of internal herniation or it could easily be prevented.

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[8] Cordonnier, J. J.: Surg. Gynec. & Obst., 88: 441, 1949.

* From his motion picture film, seen since presenting this paper, I understand that he does now extraperitonealize the sites of implantation, but there is no indication that any attempt is made to close the spaces behind the sigmoid.

[9] Mayo, C. H. and Dixon, C. F.: Ann. Surg., 87: 711, 1928.

[10] Morris, Henry: Human Anatomy. Philadelphia: P. Blakiston & Co., 1893, 1st ed., p. 1015.

[11] Coffey, R. C.: Surg. Gynec. & Obst., 47: 593, 1928.

[12] Schinagel, G.: J. Urol., 59: 1101, 1948.

However, in many reports, and especially in most recent ones, the implantations are intentionally placed higher in the sigmoid and the sites of right and left implantations are farther apart, the left being shown as at or near the distal part of the descending colon. Cordonnier[8] reports that after implanting both ureters, he rolls the sigmoid downward to produce a straightening of the ureter (left) and closing the posterior parietal peritoneum; it is not clear that he prevents the herniation here described. The illustrations in Dr. Flocks' report[2] of January 1948, do not show any mesosigmoid, but in watching him doing his operation I do not remember that he obliterated the opening behind the sigmoid. Illustrations and descriptions from other reports by Jewett[13], Jacobs,[14] Priestley and Strom,[15] Higgins,[16] Dreiling and Hyman,[17] Ferris and Priestley,[18] Schnittman,[19] Nesbit,[19] and Melick,[20] show that an internal herniation might well occur behind the sigmoid at either side of the mesosigmoid but more probably to the right, between the mesosigmoid and the point of right ureterosigmoid anastomosis (fig. 2).[18]

Of course, the best treatment of intestinal obstruction is its prevention. Prevention in these cases is by closure of the artificially made aperture by suturing. One must avoid kinking of the sigmoid and also avoid any interference with its blood supply. Closure of the peritoneal surfaces only with two rows of fine chronic catgut should suffice.

The actual occurrence of intestinal obstruction due to any internal herniation demands prompt recognition and treatment; any delay is fatal. I remember one patient some twenty years ago in whom it was necessary to resect about three feet of gangrenous bowel, although the operation was performed as soon as he reached the hospital and within 10 hours after onset of symptoms. I was recently told of a patient whose gangrenous bowel was found at autopsy, the diagnosis of mechanical intestinal obstruction due to internal herniation after a gastroenterostomy having been missed entirely; another exactly similar case recovered after prompt operation. In our case we found that reduction of the herniated bowel could easily cause tearing at the site of the recent ureteral implantation. It has been suggested that such a hazard may be avoided by emptying the strangulated bowel by trochar and suction, closing the perforation with a purse-string suture at once.

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[13] Jewett, H. J.: Brit. J. Urol., **15:** 121, 1943; J. Urol., **48:** 489, 1942.
[14] Jacobs, A.: Brit. J. Urol., **18:** 4, 1946.
[15] Priestley, J. T. and Strom, G. W.: J. Urol., **50:** 210, 1943.
[16] Higgins, C. C.: J. Urol., **57:** 693, 1947.
[17] Dreiling, D. A. and Hyman, A.: J. Urol., **58:** 435, 1947.
[18] Ferris, D. O. and Priestley, J. T.: J. Urol., **60:** 98, 1948.
[19] Schnittman, M.: J. Urol., **60:** 421, 1948.
[20] Melick, W. F.: J. Urol., **62:** 454, 1949.

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INSTRUMENT FOR ENDOSCOPIC EXTRACTION OF URETERAL STONES

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Many instruments and techniques have been described for the endoscopic removal of stones from the ureter. These may be classified into 1) methods of engaging the stone in an instrument, and removing it by traction, and 2) methods of dilating the ureter so that the stone will later pass spontaneously. The two methods have been sometimes combined; that is, a method of instrumental extraction may be used after previous dilatation of the ureter. By use of the instrument and the technique to be described, the ureter is dilated at the same time as the stone is removed. This seems to offer certain advantages which will be discussed.

The instrument consists of a Johnson[1] stone-basket which is mounted on a size 7F ureteral catheter; a Dourmashkin[2] bag is placed about 2 cm. from the junction of the catheter and basket. (See figure 1.)

The instrument is passed up the ureter with a wire stylet in the catheter lumen, after preliminary dilatation of the ureteral meatus if desired, to a position so that the basket is just past the expected location of the stone. The graduations on the catheter are of assistance in ascending the correct distance. If the stone is felt to engage in the basket, it is then pushed upwards 2 or 3 cm., the stylet removed, and the bag blown up with from 0.6 to 1.2 cc (or occasionally more) of sterile water. If the stone is not definitely felt to engage, an x-ray may be taken, to show the relationship of the basket to the stone, and the instrument manipulated until it does engage. (Figure 2 shows successive films of a stone in the ureter first identified with a catheter, then engaged in the basket, and finally after inflating the bag with skiodan solution.) The instrument is then slowly drawn down the ureter, using only the tip of one finger and the thumb for traction; forceful traction is not recommended, and should not be necessary. The inflated balloon thus dilates the ureter immediately in front of the basket with the contained stone, as it progresses down the ureter. The bag is deflated as soon as it enters the bladder. We usually carry out the procedure described under spinal anaesthesia, using a size 26F or 28F panendoscope.

DISCUSSION

The instrument described has a number of theoretical advantages; how frequently these advantages will be realized in practice is not yet clear, because the instrument has been used in only a small number of cases.

It seems established that this method of dilatation, by the inflated bag, is effective and safe, as reported by Dourmashkin[3]; there was no instance of rup-

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Read at annual meeting, Northeastern Section, American Urological Association, Bolton Landing, N. Y., September 16, 1950.

[1] Johnson, F. P.: J. Urol., 37: 84, 1937.

[2] Dourmashkin, R. L.: J. Urol., 15: 449, 1926.

[3] Dourmashkin, R. L.: J. Urol., 54: 245, 1945.

tured ureter nor of mortality resulting from instrumentation in his 1550 cases. If and when the stone can be engaged in the basket, it would appear that it can be removed with minimal trauma immediately after such dilatation, through the flaccid ureter. It seems desirable for several reasons to obtain the stone promptly, rather than to await its spontaneous passage through the dilated ureter.

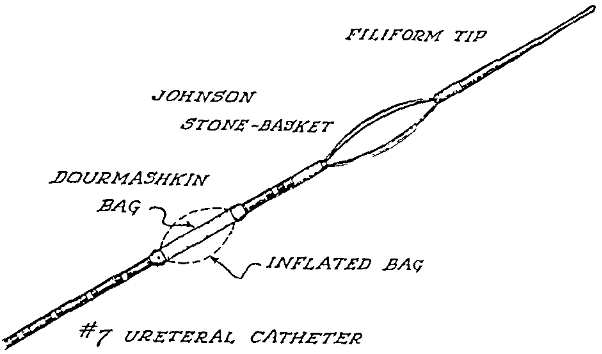


FIG. 1. Diagram of terminal portion of new instrument for endoscopic extraction of ureteral stones.

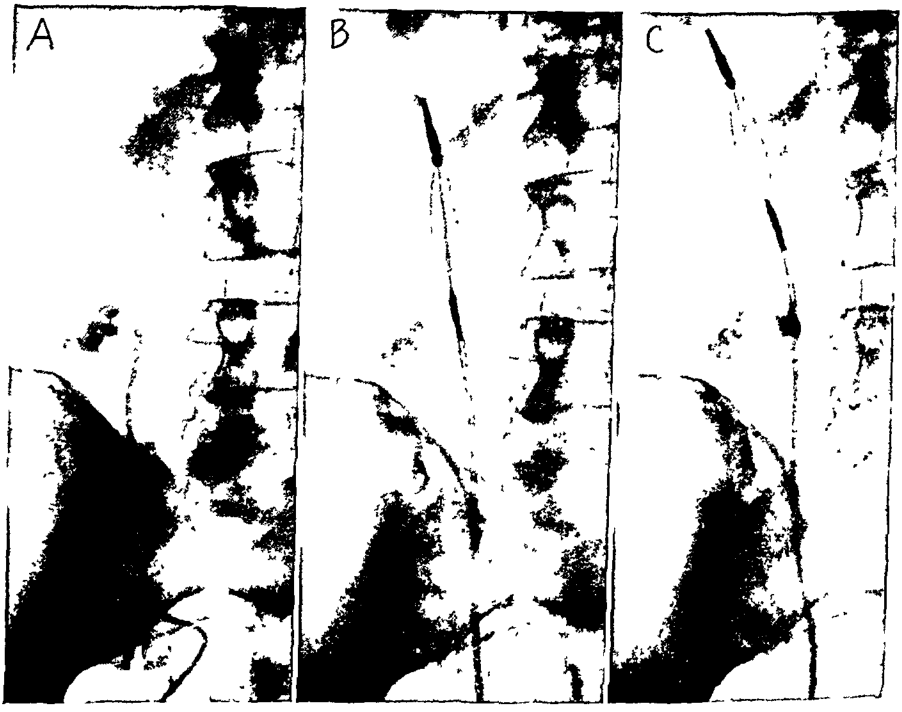


FIG. 2. *A*, showing ureteral catheter in contact with small stone in right ureter Larger area of calcium density is outside urinary tract. *B*, same patient as *A* Stone now lies in lower portion of stone-basket, and has been pushed upward about 3 cm *C*, same patient as *A* and *B* Balloon has been distended with 1 5 cc 20 per cent skiodan solution Stone cannot readily be seen in the film, but remained in basket, and was easily withdrawn from ureter

Another advantage is that the bag is not likely to be ruptured by contact with the stone after inflation, as we have found to occur at times when using the standard Dourmashkin balloon. This assumes that the stone will usually be engaged on the upward passage of the basket, and it is partly for this reason that an x-ray check is suggested, before inflating the balloon.

Various difficulties have been encountered with the instrument, including the following. Occasionally it was not possible to easily pass the instrument beyond the stone; in these we stopped, and tried again after 2–3 days interval, and were prepared to remove the stone at once, by open operation, if necessary during this period. The stone has been pushed back into the renal pelvis; when this occurred, the ureter was dilated by the inflated balloon, and the spontaneous expulsion of the stone awaited. The stone has been lost from the basket after having been engaged; in each of these cases it was recovered by passing the instrument up the ureter a second or a third time.

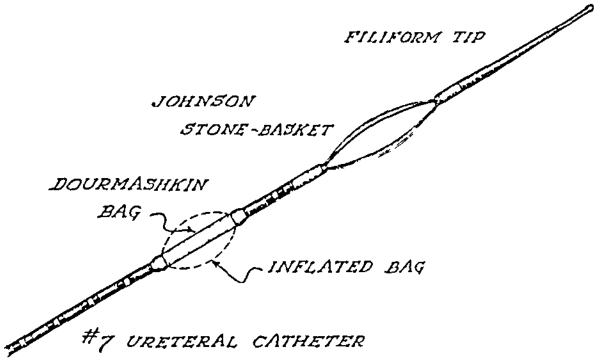
It is not the intention of the author to discuss here the merits and risks of endoscopic removal of stones from the ureter. It may be said, however, that our experience has led us to believe that the method described, using the new instrument, permits extraction of ureteral stones with less trauma and greater ease than with the standard basket, and with more certainty of obtaining the stone promptly than with the various methods of dilatation. Therefore, while we believe that open operation is preferable in many cases of stone high in the ureter, and also that many small stones in the lower ureter are best left to pass spontaneously, we now consider endoscopic extraction of ureteral stones more frequently than in the past.

SUMMARY

A new instrument has been described, which is essentially a combination of a Johnson stone-basket and a Dourmashkin bag, which appears to permit the endoscopic extraction of stones from the ureter with greater ease than heretofore, and hence with greater safety.

170 St. George St., Toronto 5, Canada

tured ureter nor of mortality resulting from instrumentation in his 1550 cases If and when the stone can be engaged in the basket, it would appear that it can



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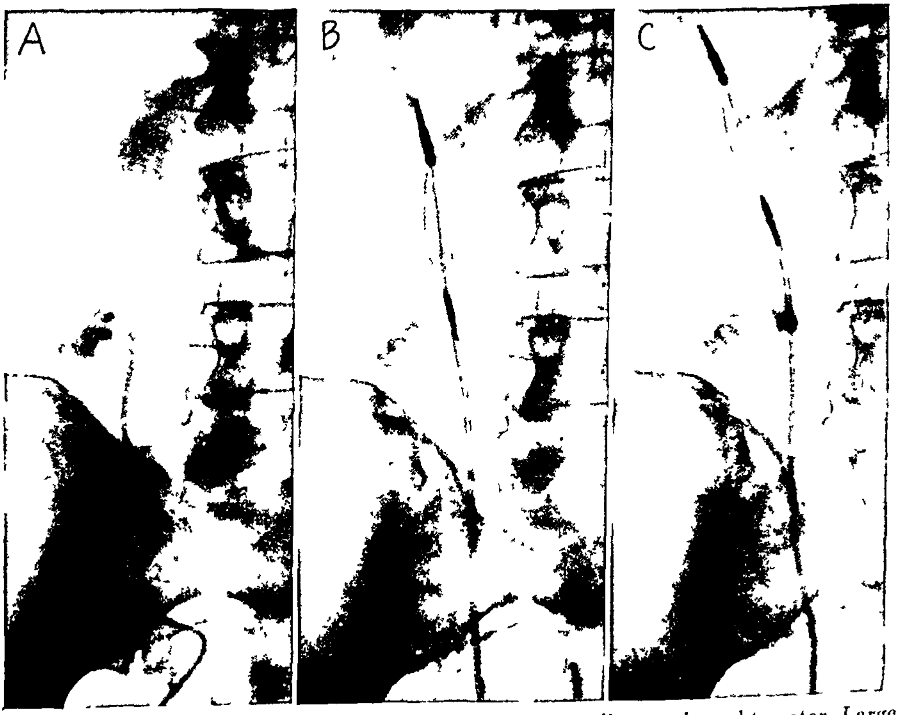

Fig 2 *A*, showing ureteral catheter in contact with small stone in right ureter Larger area of calcium density is outside urinary tract *B*, same patient as *A* Stone now lies in lower portion of stone-basket, and has been pushed upward about 3 cm *C*, same patient as *A* and *B* Balloon has been distended with 1 5 cc 20 per cent skiodan solution Stone cannot readily be seen in the film, but remained in basket, and was easily withdrawn from ureter

be removed with minimal trauma immediately after such dilatation, through the flaccid ureter. It seems desirable for several reasons to obtain the stone promptly, rather than to await its spontaneous passage through the dilated ureter.

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A "BABY" URETERAL MEATOTOME

LEANDER W. RIBA AND JAMES B. REYNOLDS

We have experienced difficulty in performing a ureteral meatotomy in children through a small caliber cystoscope. Meatotomes are usually designed for use through an operating cystoscope or urethroscope. Tightly constricted ureteral meati in adults may present extreme difficulties with standard instruments.

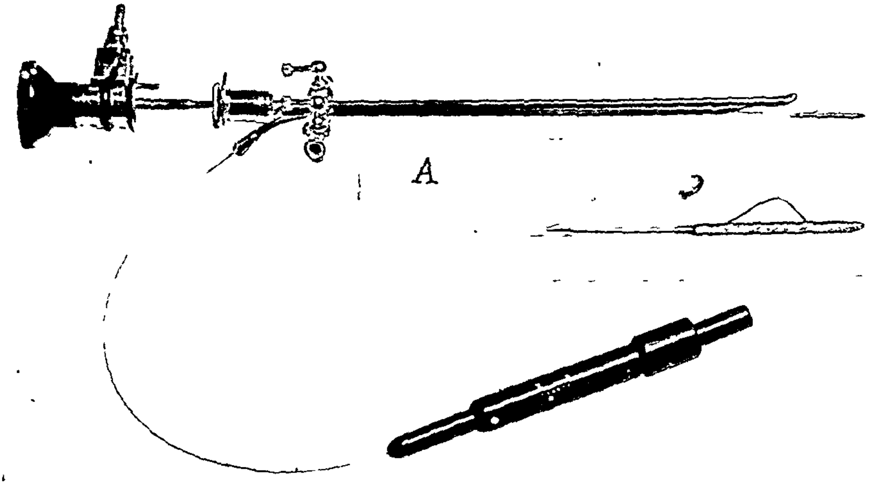

FIG. 1. "Baby" meatotome, 5F, being passed through 15F McCarthy cystoscope. Calibration on bakelite is shown. *A* shows loop extended.

The Greenwald Co. Inc. has made a baby ureteral meatotome for us, size 5F, which can be used through a 13 or 15F McCarthy cystoscope. The flexible portion is 37 cm. long and the cutting loop may be expended to a 15F.

We have found this instrument (fig. 1) most valuable in performing a ureteral meatotomy through a small or large instrument. A high frequency cutting current delivered by any standard electrosurgical unit will neatly divide the ureteral meatus. We prefer to introduce the instrument through the meatus, expend the loop and cut under vision while the instrument is withdrawn into the bladder. Excessive bleeders should be fulgurated.

720 N. Michigan Ave., Chicago 11, Ill.

Read at annual meeting, North Central Section, American Urological Association, Milwaukee, Wis., October 12, 1950.

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VESICOVAGINAL FISTULA FROM THE STANDPOINT OF THE UROLOGIST

VINCENT J. O'CONOR and J. KENNETH SOKOL

From the Departments of Urology, Wesley Memorial Hospital and Northwestern University Medical School, Chicago, Ill.

Closure of a vesicovaginal fistula should not be considered the special prerogative of any surgical specialty. Combined urologic and gynecologic judgment may be necessary in selecting the proper method of treatment.

We are fortunate in our present practice to have in operation a most satisfactory teamwork between the urological and gynecological departments of our hospital. Even the older surgeons have gradually recognized the special problem involved and usually defer to the advice of the urologist as to the proper procedures in the diagnosis and treatment of vesicovaginal fistulas.

As a result of this cooperation, careful and complete preoperative urological investigation precedes the operative attack in each instance. This study includes cystoscopic examination, ureteral catheterization, excretory and, if necessary, retrograde urography. Vesical or ureteral injections of colored solutions may demonstrate unsuspected multiplicity of fistulas. Intravenous injections of indigo carmine or methylene blue solutions may be helpful in locating the vaginal position of the fistulous orifice. It is not unusual for a patient to have more than one opening between the bladder and vagina. The presence of a large obvious fistula should not mislead the cystoscopist in his attempt to discover another smaller opening if one exists. Vesicovaginal and ureterovaginal fistulas occasionally co-exist and the double lesion should always be recognized before the operative attack is planned.

The urologist should conduct a careful examination even in the low-lying fistula resulting from an obstetrical injury. The condition may seem simple and readily amenable to the type of vaginal repair usually performed by the experienced gynecologist. Unless the gynecologist is also an experienced cystoscopist he will frequently need the help and advice of a urologist. Stress incontinence due to weakness or injury of the pubococcygeus muscle and surrounding structures may exist in the presence of a vesicovaginal fistula. This should be recognized before operation and the surgical attack planned so as to correct, if possible, both conditions at the same time.

In studying the upper urinary tract, it must be remembered that a dilated tortuous ureter is much more vulnerable to surgical injury during gynecological operations than is the normal ureter and a certain number of ureterovaginal fistulas result because a true picture of the upper urinary trees has not been obtained before surgery.

POSSIBLE PROCEDURES IN THE CORRECTION OF VESICOVAGINAL FISTULA

1) Spontaneous closure
2) Catheter drainage (nonsurgical)

Read at annual meeting, North Central Section, American Urological Association, Milwaukee, Wis., October 12, 1950.

    a) Alone
    b) After cystoscopic and/or vaginal coagulation
    c) Postural aid
  3) Vaginal closure
    a) Urethral catheter drainage
    b) Suprapubic drainage
    c) Combined urethral and suprapubic drainage
  4) Suprapubic closure
    a) Extraperitoneal
    b) Transperitoneal
    c) Combined urethral and suprapubic drainage
  5) Bilateral ureterosigmoidal anastomosis
  6) Bilateral cutaneous ureterostomy

Spontaneous closure. A small number of vesicovaginal openings will close spontaneously and many of these are probably not recognized clinically. In years long past, we have observed two instances of the relation of syphilis to the healing of vesicovaginal fistula. These are worthy of mention.

Case 1: In January 1928, a 24 year old woman stated that in August 1926, she had been delivered of her first child by forceps and had developed a vesicovaginal fistula. She had been in excellent obstetric hands and the incident had caused considerable embarrassment. In June 1927, she was operated upon by one of America's best known gynecologists. The fistula was closed for 3 weeks but reopened with complete incontinence. In January 1928, examination showed a very small fistulous opening in the bas fonde midway between the ureteral orifices. Traction on the cervix brought the vaginal opening of the fistula into excellent view. I could not understand why so competent a surgeon had failed to effect a closure and assured the patient that satisfactory closure could be made from the vaginal side.

The operation was so easy and satisfactory that no attempt was made at keeping the area dry by posture, although an indwelling catheter was retained for three weeks. The patient voided normally without leakage for 48 hours, after which time partial urinary leakage recurred from the vaginal tract. I was puzzled and discouraged at this result until my fingers fell upon an enlarged epitrochlear node which suggested an overlooked luetic condition. The blood Wassermann (previously omitted from the routine) was returned as 4 plus. Re-insertion of an indwelling catheter and intravenous arsphenamine resulted in a complete closure of the tract in 14 days. Subsequent antiluetic treatment and observation until July 1931, resulted in complete cure.

Case 2: In March 1928, with the previous experience freshly in mind, we were consulted by a Mexican girl, 19 years of age. She was completely incontinent from a small vesicovaginal fistula following her second delivery 4 months previously. The blood Wassermann was 4 plus. The fistula admitted an 8F bougie and was 0.5 cm. above and medial to the right ureteral orifice. Intravenous arsphenamine, without indwelling catheter or other local measures, resulted in complete closure of the fistula after 14 days. This patient was observed for another 2 weeks, during which time her bladder functioned normally. She then disappeared and has not been seen since.

Nonsurgical closure. Certain types of vesicovaginal fistulas which might be closed by more simple urologic treatment are frequently subjected to extensive surgical procedures. Multiple operations often reduce the size of the fistula without effecting the necessary closure that restores normal bladder function. We should like to emphasize the possibility of success in closing less extensive defects by cystoscopic and vaginal coagulation of the tract and proper prolonged postural drainage of the bladder by means of an indwelling urethral catheter. This procedure has received little or no consideration in the voluminous literature on the subject of vesicovaginal fistula. One finds no mention of it in standard texts on gynecology. In 1938, we advocated a more extensive trial of electrocoagulation for small, highly situated vesicovaginal fistulas to be followed by indwelling catheter drainage for from 2 to 3 weeks. Satisfactory modifications of the Bradford frame were sometimes used to provide postural aid in keeping the area of the fistula as dry as possible. In 1938, we reported four instances where successful closure was maintained by this method when multiple surgical procedures had failed.

During the past 12 years, we have successfully closed the fistula in this manner in 8 additional patients, 5 of whom previously had been operated upon from 1 to 5 times without permanent closure.

In 4 cases in which the patients were subjected to nonsurgical treatment in this manner, the fistulas failed to close but later success was obtained by operation. It is equally as discouraging to the patient to undergo a period of bed rest with indwelling catheter drainage and have a failure to close the fistula as when extensive surgical procedures have been employed with an unsuccessful result. For this reason, one must use his measured judgment in the selection of patients for either procedure.

Small vesicovaginal fistulas with healthy surrounding tissue will heal after electrocoagulation, if postural drainage can be maintained by an indwelling catheter for a sufficient period of time. The possibility of success by this method should receive more consideration, especially in patients upon whom an unsuccessful surgical repair has resulted in a small, lateral opening. The method obviously has no place in the treatment of fistulas of the bladder floor or where extensive tissue defect exists. During the healing period continuous acidulation of the urine should be maintained to prevent lime encrustation of the coagulated tissue. Urinary antisepsis is important in order to keep the urine sterile during the healing period. The administration of estrogens is said to favor vaginal mucosal regeneration so these are also given while the patient is in the recumbent period.

Vaginal closure. In the past, we have successfully repaired some twenty instances of vesicovaginal fistula by the vaginal route. Four of these patients had suprapubic cystotomy plus urethral catheter drainage during the healing period. In addition, there were 5 patients, all difficult cases, in whom we attempted a combined suprapubic and vaginal closure. Three of these procedures were successful and two were failures. One of these patients was cured by a vaginal procedure in another clinic and the fifth had bilateral ureterosigmoidostomy done elsewhere. This latter fistula was due to an extensive tissue breakdown following cervical irradiation.

In recent years it has been our custom to refer patients whose condition suggested the advisability of vaginal closure to one of our gynecologic associates. We believed that their more frequent dissection of the female perineum and associated structures should make for greater competence in the over-all surgical management of these patients. Occasionally we perform preliminary suprapubic cystotomy for the gynecologist.

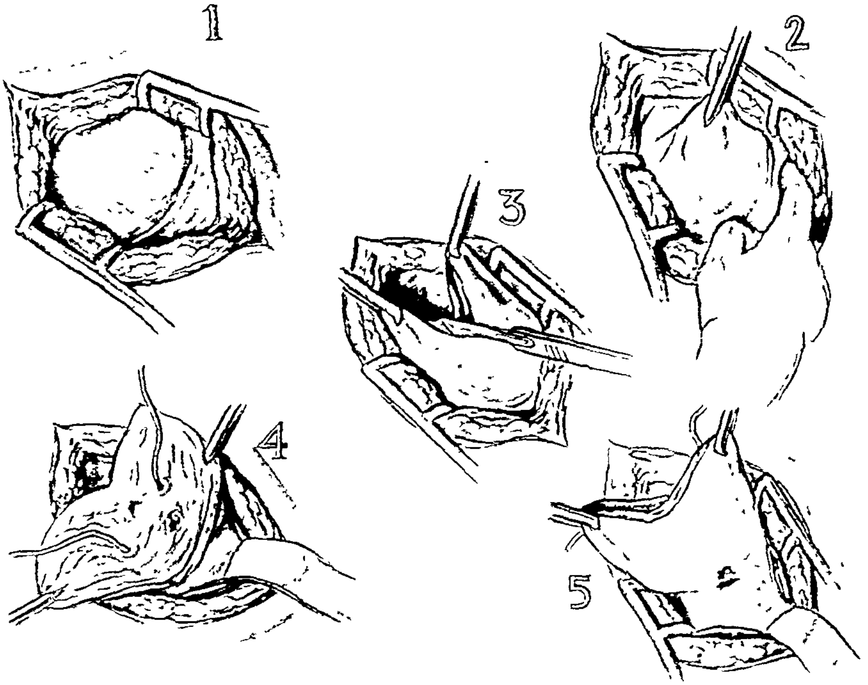

FIG. 1. *1*, Wide extraperitoneal exposure of bladder wall. *2*, Lateral bladder wall separation carried as widely as possible. *3*, Bladder dome opened widely *4*, Exposure of interior of bladder. Catheters placed in each ureter. *5*, Separation of posterior wall of bladder down to and beyond the vaginal opening.

Suprapubic closure. Many ingenious methods of suprapubic closure have been suggested and I will not detail any of them except the radical procedure about to be described. Many of these patients with vesicovaginal fistulas come to the urologist after repeated failures at the hands of general surgeons and gynecologists. (The reverse may also occur.) These patients are not good candidates for vaginal closure procedures because the fistulous opening has been gradually worked upward and away from the bladder floor, and the anterior vaginal wall has been scarred and made partly avascular.

Since 1943, we have utilized a suprapubic procedure (figs. 1, 2, 3) which employs wide separation of the posterior bladder wall, preferably extraperitoneal, with bisection down to the fistulous opening. This allows complete separation of the bladder wall from the fistulous tract in the vaginal wall and makes it relatively inconsequential whether the opening in the vagina is closed or not.

Case 1: A. O., aged 49; vesicovaginal fistula and rectovaginal fistula occurred 4 *years previously after total supravaginal hysterectomy*. Rectovaginal connection closed on first attempt 4 months after first operation. Three attempts at vaginal closure elsewhere were unsuccessful during a 2 year period. Satisfactory closure by suprapubic method.

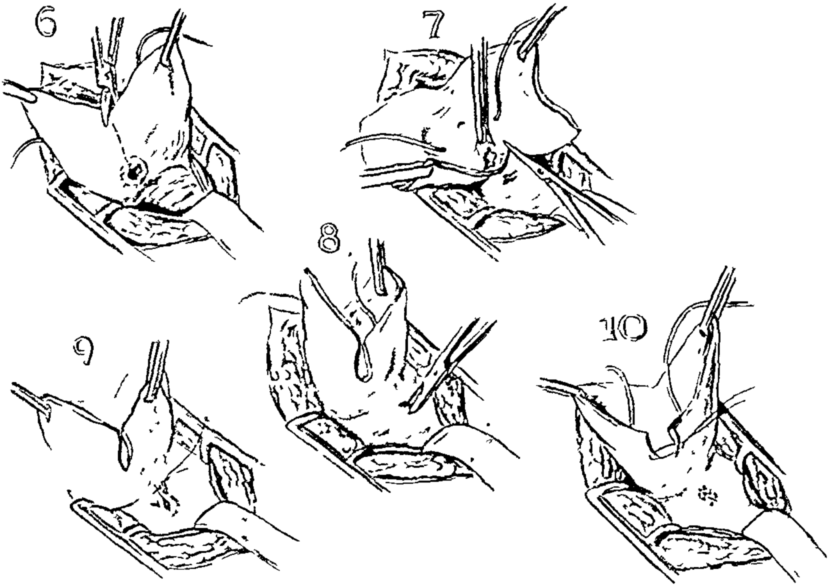

FIG 2. *6*, Bisection of posterior wall of bladder down to and surrounding vesical opening *7*, Excision of vesical area of fistula. *8*, Trimming edges of vaginal opening. *9*, Closure of vaginal wall *10*, Traction suture at base of bisected bladder wall.

Case 2: E. A., aged 53; vesicovaginal fistula after abdominal hysterectomy. Two attempts elsewhere at vaginal closure were unsuccessful. An attempt by us to close by cystoscopic coagulation and three weeks of catheter drainage was unsuccessful. Closed satisfactorily by suprapubic procedure.

Case 3: H. F., aged 24; extensive postpartum vesicovaginal fistula 2 years before. Unsuccessful vaginal closure on two occasions elsewhere. Satisfactory suprapubic closure.

Case 4: E. H., aged 52; vesicovaginal fistula of 1 year's duration, after abdominal hysterectomy. Four unsuccessful attempts elsewhere by the vaginal route in that one year. Successful suprapubic closure.

Case 5: A. W., aged 71; was seen 32 months after vaginal hysterectomy.

Vesicovaginal fistula twice operated upon elsewhere through vaginal approach with failure on both occasions. Extensive defect closed by suprapubic procedure.

Case 6: R. W., aged 49; vesicovaginal fistula of 2 years' duration after vaginal hysterectomy. Left nephrectomy 1 year later for ureterovaginal fistula. Two unsuccessful attempts at vaginal closure done elsewhere. Satisfactory suprapubic closure.

Case 7: M. McK., aged 52; vesicovaginal and enterovaginal fistulas followed abdominal hysterectomy and radiation of the cervix. Consulted us 3 years later after 2 unsuccessful vaginal procedures. A transverse colostomy was done after resection of a loop of large bowel. Six months later the colostomy was closed and 4 months after this a successful suprapubic closure was made despite all the previous surgery.

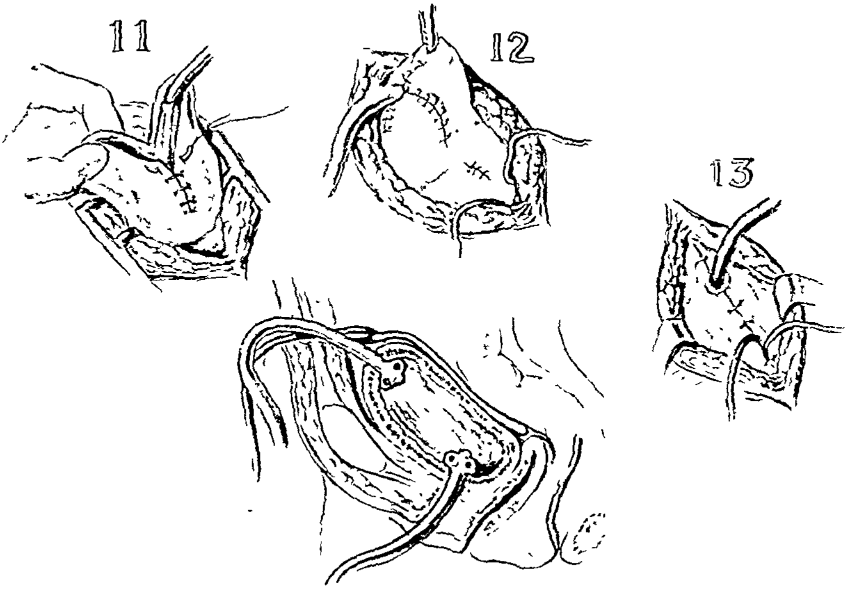

FIG. 3. *11*, Closure of bladder wall along posterior aspect. *12*, Suprapubic catheter drainage after closure of bladder wall. *13*, Closure of rectus fascia with drainage tubes left posterior to bladder wall at area of closure. Drainage both by suprapubic and urethral catheters.

Case 8: E. R., aged 47 years; vesicovaginal fistula of 4 years' duration following abdominal hysterectomy. Three unsuccessful attempts at vaginal closure and one suprapubic failure, all done elsewhere. Satisfactory suprapubic closure by the method described.

Case 9: B. S., aged 40; vesicovaginal fistula of 2 years' duration following a total vaginal hysterectomy done elsewhere. Two attempts at closure by the vaginal route at another hospital had been unsuccessful. Satisfactory suprapubic closure was attained on the first attempt.

Case 10: E. B., aged 56 years; vesicovaginal fistula occurred 3 weeks after suprapubic coagulation of a papillary carcinoma of the bladder was done by us. Due to the insistence of the patient, a suprapubic attempt at closure was attempted by us 3 months later with subsequent breakdown. Successful vaginal closure was done 5 months later by a gynecologic colleague. In this case we obviously used poor judgment in attempting the closure so soon after the causative coagulation.

Case 11: I. K., aged 55; vesicovaginal and enterovaginal fistulas after vaginal hysterectomy preceded by cervical radiation. Seen by us 3 years later. Transverse colostomy was followed by closure of enterovaginal fistula 6 months later. A suprapubic attempt at closure was unsuccessful due to the extensive defect and poor viability of the vaginal and vesical tissues from the radiation reaction. The opening is much smaller and another suprapubic procedure will be attempted later on.

This small experience with a type of procedure using bisection of the bladder wall and suprapubic closure has enabled us to close 9 out of 11 fistulas at the first attempt. All except one of these patients had had 2, 3 or 4 unsuccessful operations before coming to us. The 2 failures occurred in patients whose tissue was obviously not conditioned for closure at the time of operation.

Ureterosigmoidostomy with or without cystectomy has been done in our clinic as a palliative measure on 6 occasions. Only one of these patients is alive, well and comfortable 8 years after operation. The others have died of cancer. The relief of symptoms is worthwhile if a reasonable life expectancy exists.

Bilateral cutaneous ureterostomy has been done for 1 patient with radiation damage of the bowel which contraindicated ureterosigmoidostomy. This patient lived in relative comfort for 2 years before dying of metastatic carcinoma.

CONCLUSIONS

The urologist should take a vital interest in the problem of vesicovaginal fistula. The details of diagnosis and the indications for corrective procedures will stem from the results of a careful and complete urological examination. The possibility of nonsurgical closure should be considered before surgical measures are employed.

Either the vaginal or suprapubic route of attack should be employed depending upon the location of the fistula, the condition of the surrounding tissues and the experience of the surgeon.

Urinary antisepsis, acidulation of the urine and protection of the upper urinary tract are important adjuncts to corrective measures.

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AN OPERATION FOR THE CURE OF URINARY INCONTINENCE IN THE MALE

CHARLES J. COONEY AND GEORGE R. HORTON

It is our impression that most urologists have an attitude of resignation regarding urinary incontinence and seldom attempt operative relief of these patients. Many have called attention to the tremendous increase in the sale of Cunningham clamps since the advent of transurethral prostatectomy, and the difficulty with sphincteric control following perineal prostatectomy is also well known. Even in suprapubic prostatectomy there appears to be an irreducible minimum of these embarrassing complications and probably in due time the retropubic prostatectomist will also ruefully acknowledge his guilt in a certain number of cases.

Our experience is too brief to permit of drawing any dogmatic conclusions, but the operation here presented is easy to perform, devoid of any dangerous sequelae and we believe that in a satisfactory percentage of patients so treated the result will be good. Naturally, we do not mean to imply that this procedure is a panacea for urinary incontinence in the male but despite certain recognized shortcomings, it appears to have definite values. Attention is also called to the fact that Terence Millin of London is probably the originator of this particular technique and that Charles Uhle of Philadelphia has used it repeatedly in this country. However, reports are unpublished and because of the simplicity and apparent merit of the procedure, we believe that it should be brought to the attention of the society.

Most writers on this difficult subject of incontinence have advocated removal of tissue at the neck of the bladder (Young; Lowsley) or compression of the bulbous urethra by various methods, such as the use of gracilis muscle (Giordano; Deming; Player; and Callender) or pyramidalis muscle, used by various American and German surgeons. Plication of the bulb by use of ribbon catgut has been described by Lowsley and was also tried by Millin. Keyes and Squier in America, and Frantz in Germany sutured the posterior portions of the bulbocavernous muscle to the levator muscles on each side, thus fashioning a muscle sling which compressed the bulbous urethra sufficiently to provide control of dribbling.

We have used the fascial sling operation under discussion in 3 patients, all of whom were rendered totally incontinent as an aftermath of three different operative techniques for the relief of prostatic obstruction. The original operations, all by different men, were transurethral prostatectomy, suprapubic prostatectomy and radical extracapsular perineal prostatectomy.

Two of the patients in this small series have obtained almost complete relief from their incontinence while one must be classed as a failure, due to errors in details of the technique, to be described later in the case report of this patient.

This procedure is based on the use of two fascial strips, obtained from the fascia of the rectus abdominis muscle and use of these fascial strips to form a

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Read at annual meeting, North Central Section, American Urological Association, Milwaukee, Wis., October 13, 1950.

sling about the bulbous urethra, thus obtaining compression of the bulb and hence control of urinary dribbling.

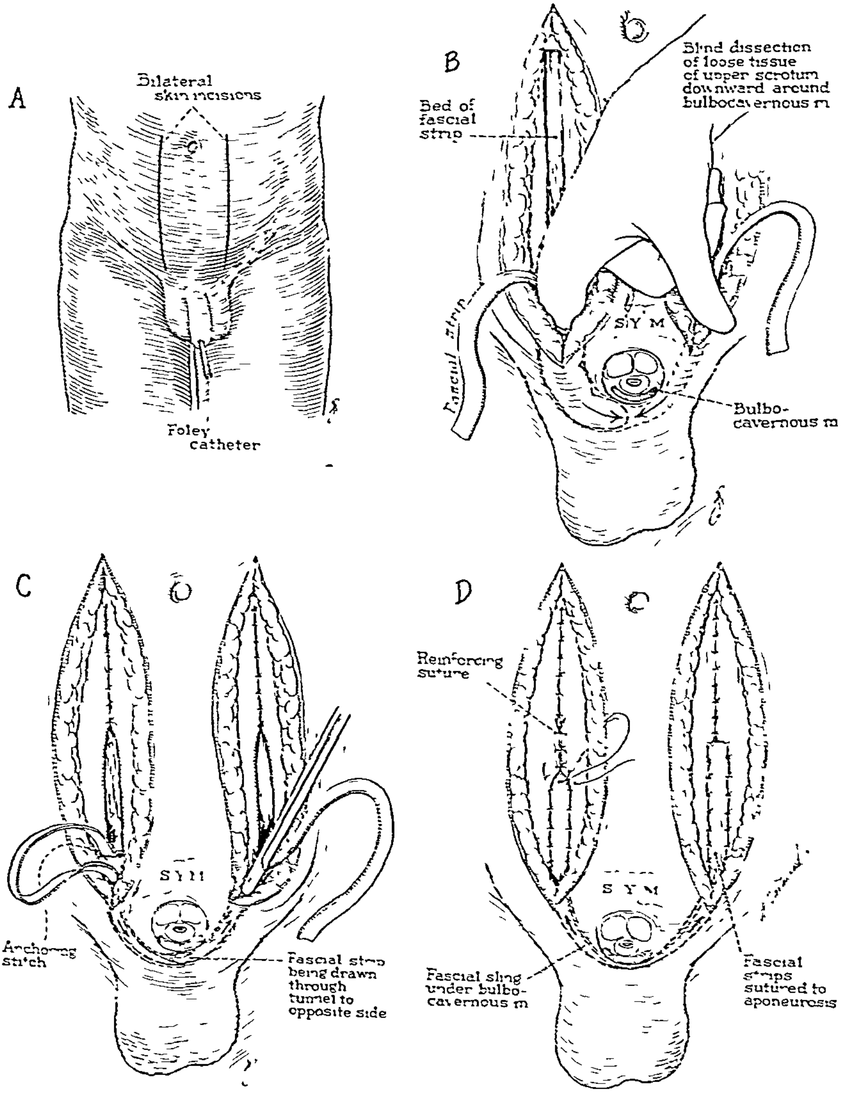
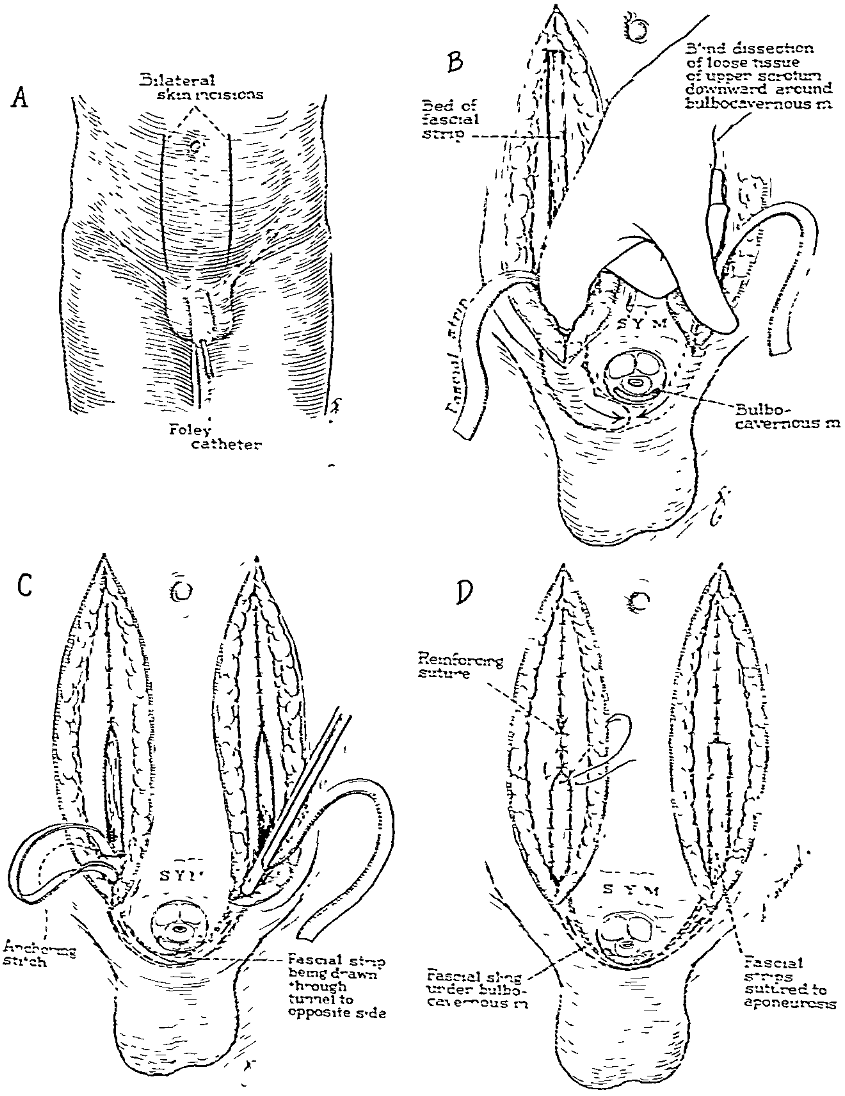

A
Bilateral skin incisions
Foley catheter
B
Bed of fascial strip
Blind dissection of loose tissue of upper scrotum downward around bulbocavernous m
Fascial strip
SYM
Bulbo-cavernous m
C
SYM
Anchoring stitch
Fascial strip being drawn through tunnel to opposite side
D
Reinforcing suture
SYM
Fascial sling under bulbo-cavernous m
Fascial strips sutured to aponeurosis

Fig. 1

TECHNIQUE

Two parallel incisions are made on either side of the midline through skin and subcutaneous tissues from just above each external inguinal ring to a point about 1 inch above the unbilicus (fig. 1, *A*). Fascial strips ¾ inch in width are obtained and freed from the muscle so each can be swung downward and crossed under

sling about the bulbous urethra, thus obtaining compression of the bulb and hence control of urinary dribbling.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Fascial sling under bulbo-cavernous m
Fascial strips sutured to aponeurosis

FIG. 1

TECHNIQUE

Two parallel incisions are made on either side of the midline through skin and subcutaneous tissues from just above each external inguinal ring to a point about 1 inch above the unbilicus (fig. 1, *A*). Fascial strips $\frac{3}{4}$ inch in width are obtained and freed from the muscle so each can be swung downward and crossed under the bulb (fig. 1, *B*). The freed strips are passed bluntly beneath the bulbous urethra and drawn up to the area of the external ring on the opposite side, where they are secured (fig. 1, *C*).

As has been illustrated, two parallel incisions are made at the sites indicated, from approximately the area of the external inguinal ring to a point just above the umbilicus. The incisions are made through the skin and subcutaneous tissue to the aponeurosis. Then two strips of fascia about ¾ inch in width are cut from the aponeurosis and freed from the rectus muscle fibers. The fascial strips are raised in the same manner as a flap graft and the cut edges of the aponeurosis are closed by suture, the material used depending upon the choice of the operator, both for this and the final placement suturing of the strips. Tantalum wire was used by the authors. The flaps are cut free at the upper ends and left attached at the lower ends. They are next swung down over the pubis and under the bulbous urethra and brought up to the aponeurosis near the external ring on the opposite side, where they are fixed by suture.

The index finger is used to blindly dissect the loose tissue of the upper scrotum and down around the bulbocavernous muscle and this is accomplished quite easily, except when there is scar tissue in the perineum from former surgery or suppuration. When the finger can be passed about the bulb a curved forceps, such as a renal pedicle clamp, is used to draw through the fascial strip from the opposite side. It is fitted about the bulb and drawn up over the pubis, where it is sutured to the aponeurosis, in the area where its fellow of the opposite side has been reflected downward.

The operator must palpate the area of compression over the bulbous urethra carefully and adjust the fascial slings for the proper degree of compression before placing the fixation sutures in each distal end of the strips, as the crux of the procedure is to accomplish enough compression of the bulbous urethra to prevent dribbling and yet to allow the patient to empty his bladder, using somewhat more force than normal in the act of micturition. It should be emphasized that the more posterior on the bulb that one can place the compressing strips, the better the end result. No drainage tubes are used and the two parallel skin incisions are closed with interrupted nonabsorbable sutures. A Foley bag catheter is in the urethra throughout the procedure and is left in situ for 5 or 6 days postoperatively.

CASE REPORTS

Case 1. A white man, aged 74, hospital number 50-3112, was first seen by us in March 1950. He had total loss of urinary control. The patient had undergone transurethral prostatic resection elsewhere in November 1948. The pathological report was adenocarcinoma of the prostate. One week later a second resection plus bilateral orchiectomy was done. From the time of the second operation he had been totally incontinent. He had good sphincter control prior to the above procedures, his presenting complaints having been only increased frequency and a slowing urinary stream. Sixteen months thus had transpired during which time the patient had used either a leg strap urinal bag or an incontinence clamp continuously.

The prostate was 1.0 plus to 1.5 plus enlarged, slightly irregular, not tender, but firm and fixed at the base just beneath each seminal vesicle. Urethral calibration failed to disclose stricture and a 24F Van Buren sound was passed to the bladder without evidence of obstruction. Residual urine was ½ ounce. The urine showed a trace of albumin and a few scattered white blood cells. Neither kidney was palpable and there was no tenderness in the flank. Excretory urograms showed normal functioning kidneys on both sides with normal morphology. Hypertrophic changes were found in the lumbar spine, but no evidence of metastatic lesions in any of the bones. Urethroscopy showed avascular-appearing, whitish, cicatricial tissue distal to the verumontanum on the roof of the urethra. No obstructing tissue was present.

The patient was admitted to the hospital on April 23, 1950. The blood count was normal, as were the urea and creatinine determinations. Serology was negative. The urological diagnosis was total urinary incontinence, secondary to external sphincter trauma incurred during the process of transurethral resection.

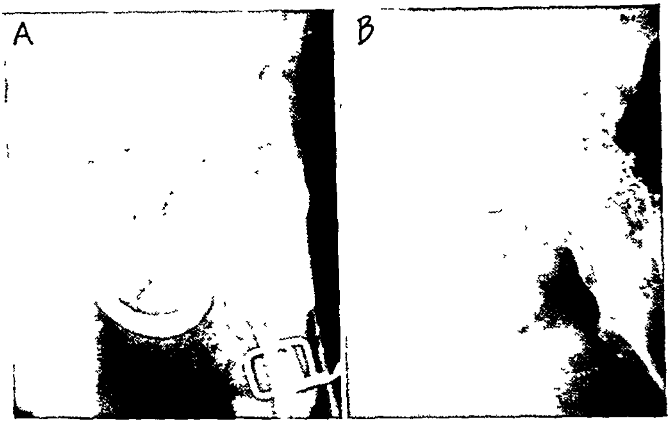

FIG. 2. *A*, urethrocystogram with clamp on penile shaft. Contrast medium easily introduced into bladder. *B*, urethrocystogram 5 minutes after removal of clamp. No contrast medium in urethra distal to point of compression. However, bladder and proximal urethra well filled with dye to point of compression.

On April 25 this patient was treated surgically by the formation of a fascial sling as described. The postoperative course was uneventful. The patient was ambulatory after the first postoperative day and on the sixth postoperative day the catheter was removed. He was able to void with ease by bending forward slightly while standing with the knees flexed.

The patient has been followed at 2 weekly intervals and has continued to do well. Residual urine has been less than one ounce. He has stated that he can void more easily by standing and leaning forward with the knees flexed than by sitting down and leaning forward. He has demonstrated that he can assume the position of full knee flexion with the buttocks resting on the heels and does not leak urine. He is completely dry while walking or sitting. Seven weeks after operation urethrograms were made (fig. 2). The healed incisions are shown in figure 3.

Case 2. A white man aged 65, hospital number 47-1197, was first seen in February 1947. He had been catheterized twice daily for the previous 4 days because of inability to void and had complained of a slow stream with loss of force and dribbling for 8 months. Continuous catheter drainage was established and the patient admitted to the hospital. He had no other urological complaints and he had suffered from no major illness during his life. He had had no operations.

The catheterized urine was clear but deeply concentrated. The prostate was 3 plus enlarged, smooth, elastic though slightly firm, movable, not tender and clinically benign. Neither kidney was palpable and there was no flank tenderness. Excretory urograms showed good functioning kidneys bilaterally with some relaxation of the calyceal and pelvic architecture, but with no marked abnormalities. The blood count, blood urea, creatinine and blood sugar were all within normal limits and the serology negative. Urethroscopic examination revealed a tri-lobar prostatic enlargement with accompanying trigonal thickening and moderate muscular trabeculation but no other abnormalities.

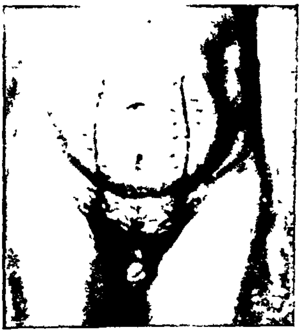

Fig. 3. Showing healed incisions

On February 22, 1947 a one-stage suprapubic prostatectomy was done by one of us (C.J.C.), the gland being enucleated with ease and removed in toto. Rather brisk initial bleeding ensued and 5 oxycel packs were snugly placed in the prostatic cavity. The pathological report was benign prostatic hyperplasia. Postoperative course was good with the exception of some inability to control urine per urethram after the wound was healed and micturition resumed. This complaint continued for the next 2½ years and it seemed probable that the sphincter muscle had been damaged, possibly by the sustained pressure of the rather tight oxycel packing, a method which we discarded after this unfortunate experience.

The patient was seen numerous times in our office since 1947, but dilatation with large size sounds and also the Kollmann dilator afforded very little relief. Ephedrine hydrochloride capsules helped some but he continued to wear an incontinence clamp. He was not totally incontinent, being dry at night, but leaked continuously when on his feet.

In July 1950, he was readmitted to the hospital with the diagnosis of incomplete urinary incontinence, secondary to suprapubic prostatectomy.

On July 3, 1950 the fascial sling operation was performed. The postoperative course was satisfactory, with no complications. The patient was allowed out of bed on the third day and the catheter removed on the sixth day following operation. The patient was released from the hospital on the ninth postoperative day. He was satisfied and declared himself almost 100 per cent cured. He has only been seen twice since leaving the hospital. He feels well and is happy and has thrown away his incontinence clamp. He drips very slightly in the act of sitting down, but is dry at all other times. He is able to void easily by leaning forward while standing. His general health is definitely better and his attitude toward life is immeasurably improved. We could not get this patient to return for follow-up urethrocystograms.

Case 3. A white man, aged 81, hospital number 50-4729, underwent radical perineal prostatectomy, including removal of seminal vesicles, elsewhere 3 years previously because of clinical diagnosis of carcinoma, which however was not substantiated by the pathologic report of the tissue. Total urinary incontinence followed this operation.

The patient was admitted to St. Joseph Hospital, Fort Wayne, Indiana on June 13, 1950. Rectal palpation revealed a smooth fibrous prostatic area. The residual urine was 10 cc. Calibration of the urethra revealed no strictures and the posterior urethra admitted sounds up to 30F inclusive with ease. Urinalysis was normal except for faint trace of albumin. The blood count was within normal limits. The blood urea nitrogen was 26 mg. per cent, blood creatinine 2 mg. per cent. Excretory urograms demonstrated normally functioning upper urinary tracts. Cysto-urethroscopic examination disclosed that the bladder mucosa was normal in appearance, the outlet not contracted, the prostatic urethra short, no nodules or other persisting obstructions, and that the area of the cut-off muscle was smooth with no abnormalities visible.

On June 15, 1950 the fascial sling operation was performed. In this instance the fascial strips were drawn considerably tighter about the bulbous urethra than in the preceding cases and this probably initiated the train of circumstances resulting in failure of the operation. It was also found later that the fascial strips were more anteriorly placed on the bulb in this patient than in the preceding 2 cases.

The indwelling catheter was removed 13 days postoperatively but urination was accomplished only with marked straining and difficulty. Twenty-four hours after removal of the catheter, bulging was noted about the suprapubic area on the right side and urine began to leak from lower extremity of skin incision on right side. The patient was taken to the operating room and a linear incision made in lower left groin and upper left scrotum, thus avoiding the tissue on the right which had been invaded by the urinary extravasation. The area of fascial sling about bulbous urethra was located and the attachment of fascial strips in left groin severed. The bands were freed from the bulbous urethra and a slough demonstrated in the urethral wall, at the point where the fascial bands had tightly compressed it over the indwelling catheter. A 20F sound was first introduced to the bladder, after which an 18F Foley bag catheter was passed to the bladder and left in position for drainage. The fascial strips were re-adjusted snugly about the bulbous urethra and resutured to the fascia overlying the pubic bone in the left groin, tantalum wire being used. A Penrose drain was placed to the area of the urethral defect and brought out through a stab wound.

Following this corrective procedure the catheter was maintained in position for a prolonged period, to allow the urethral defect to heal and the patient was discharged from the hospital July 18, the catheter being still in place. Unfortunately, the incontinence has persisted since removal of the catheter and healing of the urethral slough and despite our re-adjustment of the fascial strips, the result is an apparent failure.

SUMMARY

A simple procedure for the cure of urinary incontinence in the male is presented.

Two patients were cured by the use of fascial strips to form a sling for compression of the bulbous urethra. One failure resulted from overzealous tightening of the fascial slings, resulting in pressure necrosis of the urethral wall and urinary extravasation. Drainage was instituted, the fascial slings freed, re-adjusted and resutured in position but the incontinence has not been improved in this patient.

No claim of originality is made, but it is believed that the operation merits more widespread use among urologists.

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VOIDING CYSTO-URETHROGRAMS

J. G. SICELUFF

To the urologist a method of obtaining cysto-urethrograms under physiological conditions is a valuable diagnostic procedure. Voiding cysto-urethrograms made by filling the bladder with contrast medium and then exposing x-ray film during the act of urination have been used for this purpose. In 1913, Uhle and McKinney made x-ray films of the urethra during urination in the anteroposterior position. Several techniques have since been described. This paper will review a method which has consistently satisfied our requirements for cysto-urethral investigation. Illustrative cases are presented (figs. 1 to 9).

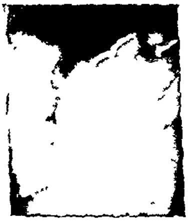

Fig. 1

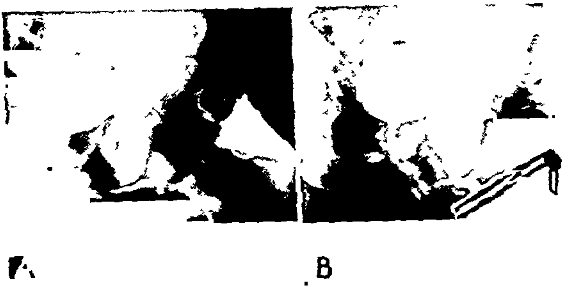

Fig. 2

Fig. 1. Case 1. Normal voiding cysto-urethrogram in healthy subject 30 years of age. Patient voiding freely. Smooth, symmetrical bladder outline; prostatic, membranous, bulbous and anterior urethra well shown.

Fig. 2. Case 2. *A*, voiding cysto-urethrogram. Normal bladder outline. Internal urethral outlet normal. Severe inflammatory stricture at bulbomembranous junction with destruction of normal contour of bulb and dilatation of membranous urethra above stricture. Prostatic ducts filled while patient voids freely. Sinus in anterior urethra shown. *B*, voiding cysto-urethrogram with patient voiding against penile clamp. Additional distention of urethra seen only below point of stricture.

The technique used was developed with Dr. John W. Draper of New York City in 1943. We started our work in an attempt to visualize the bladder and the urethra during the act of urination. At first we made films with the patient voiding immediately after excretory urography had been done. A physiologic demonstration was obtained in this way, but the films were unsatisfactory because the contrast medium voided was not of sufficient density. We developed the following procedure which has given satisfactory results.

After voiding, the patient is placed supine on a tilt radiographic table. A soft rubber catheter is passed, and the residual urine is measured. The bladder is then gently distended with air until the patient expresses a desire to void or complains of discomfort. The first film of the series is then exposed in the right posterior oblique projection and constitutes an air cystogram.

After evacuation of the air the bladder is filled with a contrast agent until a normal desire to urinate is experienced. The urethral catheter is then removed,

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Read at annual meeting, South Central Section, American Urological Association, Tulsa, Okla., September 26, 1950.

bladder and left in position for drainage. The fascial strips were re-adjusted snugly about the bulbous urethra and resutured to the fascia overlying the pubic bone in the left groin, tantalum wire being used. A Penrose drain was placed to the area of the urethral defect and brought out through a stab wound.

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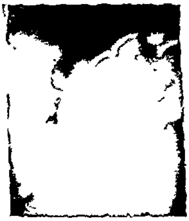
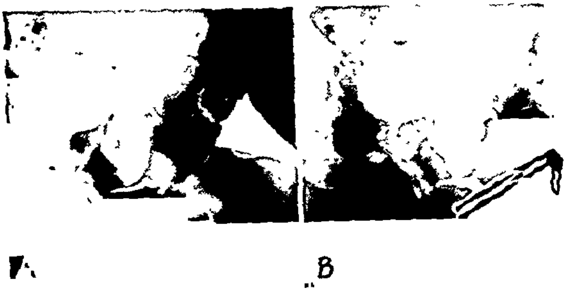


FIG. 1



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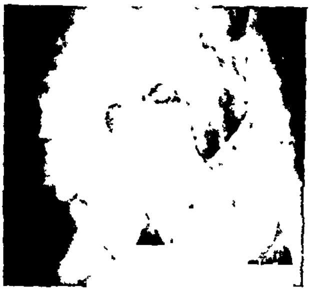

FIG. 3

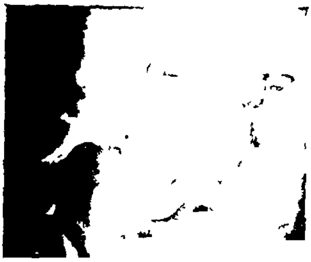

FIG. 4

FIG. 5

FIG. 3. Case 3. Voiding cysto-urethrogram. Incomplete paralysis of bladder secondary to gunshot wound, lower spine. Foreign body seen at level of fourth lumbar vertebra. Patient attempting to void. Sagging, bulging deformity of bladder. Incompetent, dilated internal urethral outlet. Stream controlled by external sphincter.

FIG. 4. Case 4. Complete paralysis, sacral plexus of nerves supplying bladder, genitalia, perineum and rectum, result of shell fragment wound, left buttock. Partial urinary and rectal incontinence. Cysto-urethrogram made 1 year after injury. Patient attempting to stop voiding. Cysto-urethrogram demonstrates incompetency of internal urethral sphincter. Residual medium in bulbous urethra. Vesical outlet is relaxed. Sagging deformity of bladder again seen. Anterior deformity of bladder shown is persistent finding in cases of this type. (*J. Urol.*, *53*: 539–544, 1945.)

FIG. 5. Case 5. Severe traumatic stricture of urethra secondary to fracture of pelvis. Film made 13 months following injury. Patient voiding freely. Urethra dilated through 26F. Persistent deformity at bulbomembranous junction. (*J. Urol.*, *53*: 539–544, 1945.)

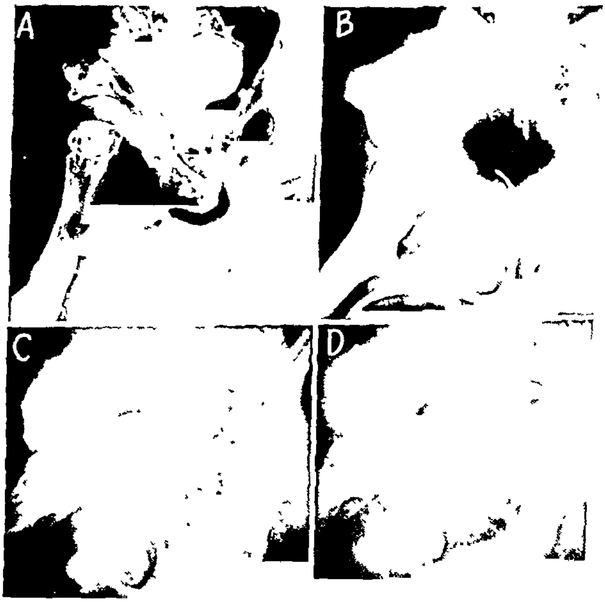

FIG. 6. Case 6. *A*, retrograde filling of urethra and bladder. Bladder filled through suprapubic tube. Complete occlusion of prostatic and membranous urethra secondary to fracture of pelvis. *B*, normal air cystogram, catheter indwelling, 8 weeks following operative repair. *C*, voiding cysto-urethrogram revealing deformity of vesical outlet and prostatic urethra. Membranous and bulbous urethra adequate. *D*, patient attempting to stop voiding. Demonstrating incompetency of internal urethral outlet.

and the table is tilted to a vertical position. The patient is again placed in the right posterior oblique position, and the right foot is now elevated approximately

15 inches. The second film is exposed while the patient is voiding freely into a vessel held in his right hand. As soon as the film has been exposed the patient is asked to stop voiding, and a third film is then promptly exposed while the urinary stream is cut off. He is then asked to void once more; and after the stream is full and strong a penis clamp is applied and the patient is urged to continue the attempt to urinate. A fourth film is exposed at this time. The clamp is removed, and the patient is requested to empty his bladder. After this is done a final exposure is made. Variations in the routine procedure are made when indicated. This technique was reported at the St. Louis meeting of the American Urological Association in 1944.

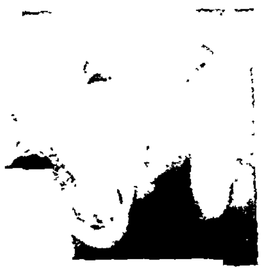

FIG. 7

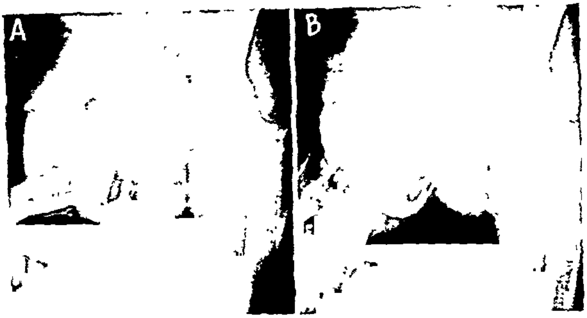

FIG. 8

FIG. 7. Case 6. Voiding cysto-urethrogram. *Patient voiding against clamp accentuates* deformity of urethra and vesical outlet previously demonstrated. Urethra distended down to point of clamp. No evidence of remaining stricture.

FIG. 8. Case 7. Voiding cysto-urethrogram. Patient voiding against obstruction. Severe traumatic stricture. Postoperative repair after membranous and prostatic urethra had been completely occluded for 4 years. Deformity of prostatic and membranous urethra *demonstrated.* Bulbous and anterior urethra distended to point of clamp. Fixed deformity in membranous area. Urethra claibrated at 16F. Blind pouch at site where urethra was originally torn.

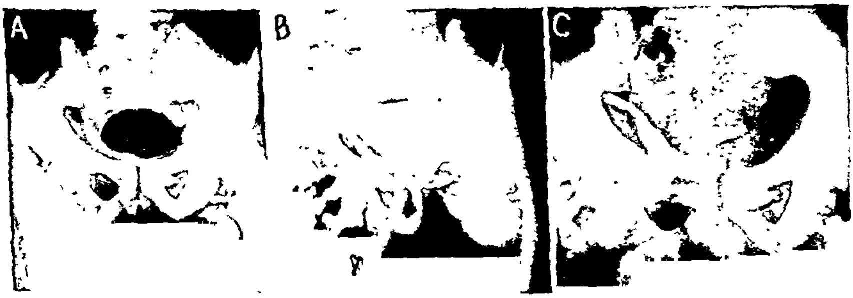

FIG. 9. Case 8. *A*, air cystogram made in anteroposterior projection. Urinary sinus, right hip. Extensive destruction of bone secondary to multiple shell fragment wounds incurred 1 year before film was made. *B*, voiding cysto-urethrogram against penile clamp. Normal urethra and bladder outline. Extensive extravasation of contrast medium through urinary sinus taking origin from base of bladder. Patient voided freely from sinus in right hip. *C*, film exposed after patient had completely emptied bladder. Small amount of residual contrast medium seen in bladder. Urethra completely emptied. Residual contrast medium in urinary sinus shown. Attempts to demonstrate this lesion by retrograde cysto-urethrography were unsuccessful before and after films shown.

Cysto-urethrograms made by this method have several advantages. The picture of the urinary tract which is obtained is a more truly physiologic one than will be had by retrograde filling. The patient suffers no discomfort provided a nonirritating contrast medium is used. Sodium iodide or bromide is irritating and will cause pain. Skiodan, 20 per cent, is a satisfactory medium. It is easy to obtain good urethrograms by this method. We have had no complications. The films are useful in demonstrating the competency of the sphincters of the bladder. It is necessary to have a cooperative patient. Selected films from cases studied by this technique demonstrate the diagnostic and illustrative value of the procedure.

SUMMARY

A simple and easy method for demonstrating pathologic lesions of the urethra and bladder on the x-ray film has been shown. The technique should be varied to suit the individual case. It has been used for seven years without complication or undue reaction.

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REFERENCES

Brodny, M. L. and Robins, S. A.: Enuresis. Use of cysto-urethrography in diagnosis. J. A. M. A., **126**: 1000–1006, 1944.

Draper, J. W. and Siceluff, J. G.: Excretory cysto-urethrograms. J. Urol., **53**: 539–544, 1945.

MacNish, J. M.: Cysto-urethrography in the male. Urol. & Cutan. Rev., **40**: 77, 1936.

Millin, T.: Retropubic Urinary Surgery. Baltimore: Williams and Wilkins Co., 1947, pp. 203–205.

Ney, C. and Duff, J.: Cysto-urethrography. Role and diagnosis of neurogenic bladder. J. Urol., **63**: 640–652, 1950.

Uhle, A. and McKinney, W.: Observations upon mechanisms of urination. Urol. & Cutan. Rev., **1**: 275, 1913.

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A NEW RECORDING CYSTOMETER

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Cystometry is a valuable adjunct to the proper diagnosis and treatment of a dysfunction of the urinary bladder. Since the introduction of this method of study in 1927 by Rose, many able investigators have added much to our knowledge concerning the pathology of the bladder. Many different types of instruments for recording changes in intravesical pressure have been described. These have varied from the simple water column manometer to extremely complex apparatus. Regardless of the instrument which one utilizes, its primary function is to reveal

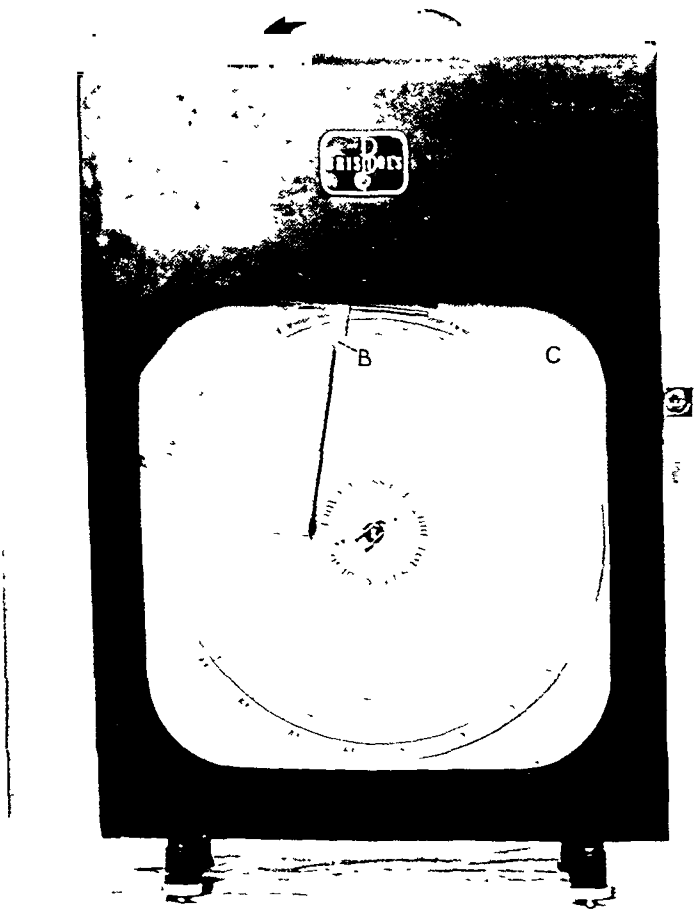

Fig. 1. Recording machine with hinged door closed. Pen arm, *B*, is in recording position on circular chart, *C*.

changes in intravesical pressure as they occur with known volumes of fluids in the bladder. Experience has shown that a recording instrument is more desirable than a nonrecording one for it provides the complete pressure change pattern as the bladder is slowly filled with fluid, while the nonrecording instrument cannot possibly do this. Many nonrecording instruments have been described and none would seem to possess any particular advantage over the other. The Lewis cystometer, the Rose cystometer, and the Landes electrocystometrograph are the recording instruments which are most widely utilized. The complex smoked-drum systems are rarely used clinically because they are too difficult to operate in a busy urologic clinic.

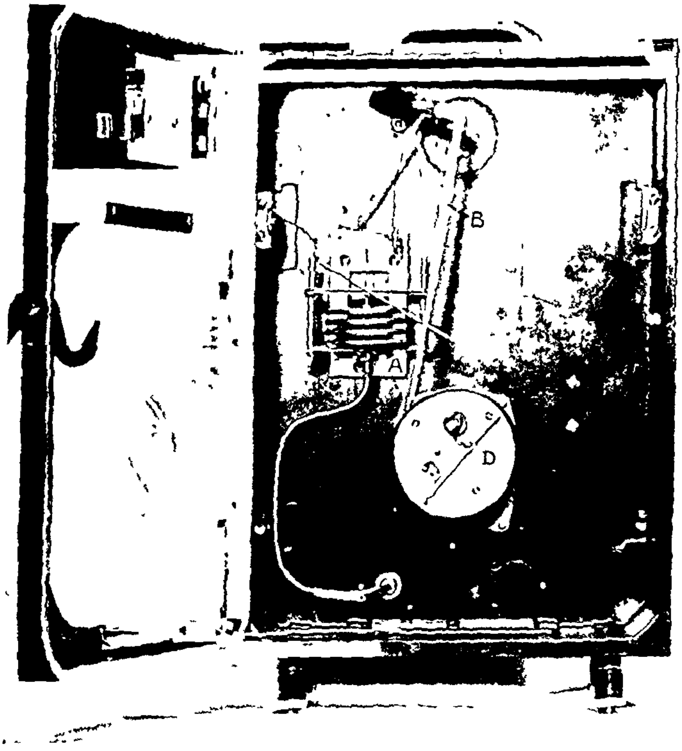

FIG. 2 Chart holding plate has been removed to show recording mechanism. Phosphor-bronze pressure diaphragm, *A*, is mechanically linked to pen arm, *B*. Two-speed spring clock mechanism, *D*, rotates chart in either 2 or 8 hours.

We have applied a relatively inexpensive, portable, and rugged industrial pressure recording gauge to clinical cystometry which records in centimeters of water rather than in millimeters of mercury. It is very compact and simple to operate. The essential parts of the instrument (fig. 1) consist of a metal case which houses a phosphor-bronze diaphragm pressure measuring element (fig. 2, *A*) linked to a stainless steel recording pen arm (fig. 2, *B*). The latter records intravesical pressure fluctuations upon a 12 inch circular chart (fig. 1, *C*) which has been calibrated from zero to 200 cm. water pressure and time in minutes. The chart is rotated by a two speed spring clock mechanism (fig. 2, *D*) which can be set to rotate the chart completely in either two or eight hours. While our instrument utilizes the above chart rotation speeds, many other chart drives are available. Likewise identical machines are available with various pressure ranges and chart diameters, however the pressure range from zero to 200 cm. of water has proved to be very satisfactory to us. As the machine is delivered one must construct a pressure transfer mechanism to convert it into a cystometer. The pressure transfer mechanism has been constructed as illustrated in figure 3 and securely mounted to the back of the instrument with metal brackets. It consists of a 50 cc syringe which serves as the method for transferring water pressure to air pressure. A syringe of this size is necessary because the fluid volume exchange necessary to affect a pressure of 200 cm. of water is approximately 50 cc. A two way stopcock (fig. 3, *F*) with a 5 mm. bore is fitted into the syringe with a rubber stopper and securely held by a metal bracket. One arm of the stopcock (*G*) is connected to a catheter in the bladder by a rigid rubber or plastic tube while the other (*H*) serves to drain the air chamber of excess fluid as one fills the entire system and is eliminating air bubbles. Upon the tip of the syringe we have placed a small two-way metal stopcock (*I*) with one arm open to the atmosphere and

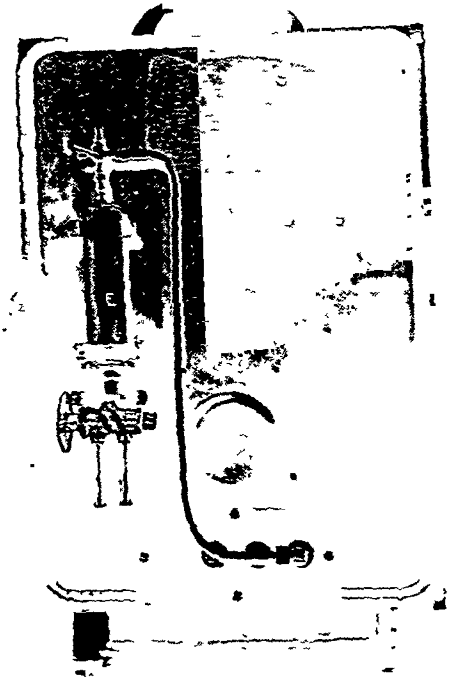

FIG 3 Pressure transfer mechanism is shown mounted to back of instrument case. Fifty cubic centimeter syringe is linked to recording mechanism by large glass two-way stopcock, *F*, and smaller metal stopcock, *I*. This arrangement facilitates fluid to air transfer of pressure from bladder to pressure element. Tubing from bladder is attached either to stopcock arm, *G*, or *H*.

the other connecting to a copper tube of 5 mm. bore which leads to the pressure diaphragm.

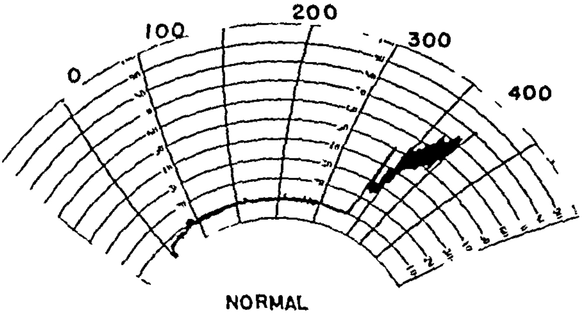

FIG 4 Normal cystometrogram Intravesical pressure maintained constant 10 cm water pressure until volume of 325 cc had been introduced Patient then experienced desire to void, and pressure rapidly rose to 70 cm water and maintained itself at that level

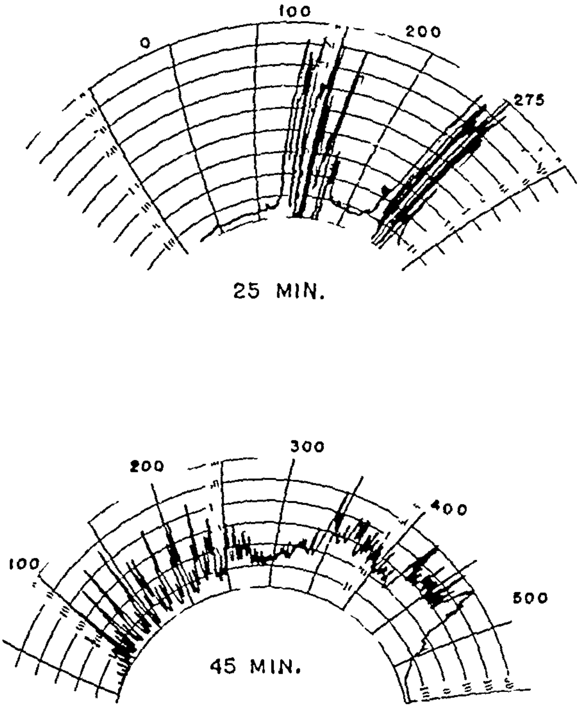

FIG 5 Upper recording made in case of paraplegic with reflex (automatic) neurogenic bladder He previously had sustained compression fracture of D 12 with transection of spinal cord While patient is not conscious of desire to void, bladder empties itself automatically at volume of approximately 300 cc No residual urine or infection present

Lower recording made in case of 43 year old woman with multiple sclerosis Uninhibited neurogenic bladder Rhythmic contractions occurred throughout filling and each contraction was accompanied by desire to void Cystogram shows bilateral vesico ureteral reflux with hydro ureter and hydronephrosis

The patient is placed upon an examining table and a hard rubber catheter is placed in the bladder The instrument is placed upon a small table equipped with an adjustable top which may readily be elevated or lowered. An adjustable operating room stool serves this purpose quite well. Adjustment of the height of the recording machine is necessary in order to obtain a zero reading of the pen arm upon the circular chart. One angle of a glass Y-tube is inserted into the urethral catheter and the latter is clamped with a hemostat. Hard rubber tubing is used to connect stopcock arm (*G*) to the Y-tube. Fluid input tubing from a 1000 cc Kelly bottle with a Murphy drip chamber connects to the remaining arm of the glass Y-tube. The entire system is then easily filled with fluid by manipulating the stopcocks (*F*) and (*I*).

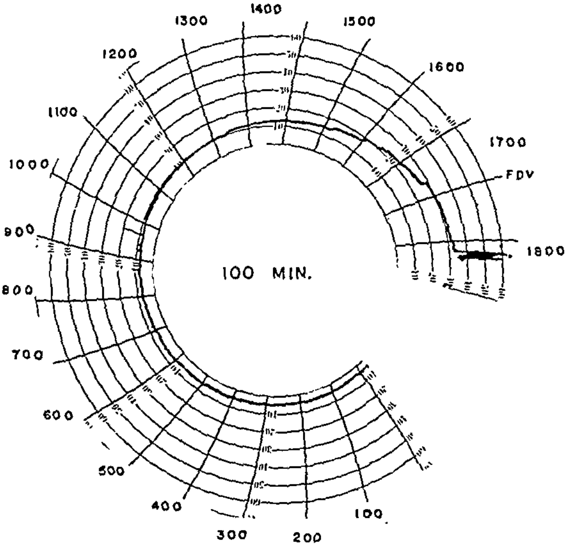

Fig. 6. Recording made in case of 45 year old tabetic with no urinary symptoms other than absence of desire to void. No residual urine. Over period of 100 minutes, bladder was filled with 1800 cc water. Maximum pressure 60 cm. water.

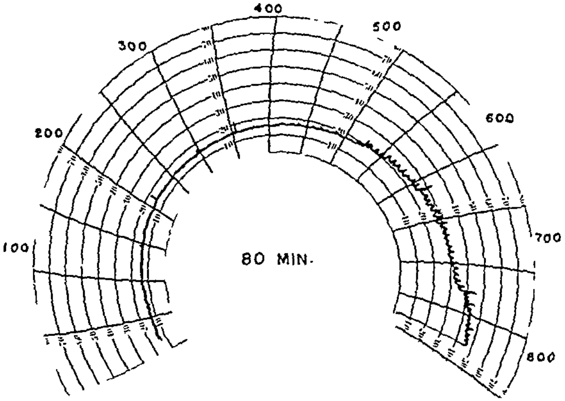

Fig. 7. Recording made in case of 40 year old woman with severe arachnoiditis following spinal anesthesia. Complete absence of both sensory and motor function resulting in autonomous neurogenic bladder.

A resting fluid level is allowed to remain in the air chamber (*E*) and stopcock (*I*) is closed. The clamp is next removed from the urethral catheter and the pen arm is adjusted to a zero reading by elevating or lowering the table upon which the instrument rests. Fluid is allowed to drip very slowly into the bladder and as each change in intravesical pressure occurs it is continuously recorded upon the circular chart. Appropriate comments may readily be added to the chart with a pen or pencil. When the recording is completed the chart is removed from the machine and preserved as a permanent record (figs. 4, 5, 6 and 7). With the clock set to rotate the chart once in 8 hours one is able to do direct cystometry without adding fluid to the bladder. A comparison of eight hour cystometric recordings with the conventional type of cystometrograms will be the subject of a later report.

SUMMARY AND CONCLUSIONS

We have used as a practical clinical cystometer an inexpensive industrial pressure gauge which records in centimeters of water.

This instrument is sturdily constructed, compact, completely portable, and is simple to operate.

Utilizing the 8 hour chart drive, one will be able to do direct cystometry without adding fluid to the bladder.

Since a water recording instrument is 13.5 times as sensitive as a mercury recording machine, this cystometer will be valuable in the study of effects of various pharmacologic agents upon the urinary bladder.

The air chamber can easily be eliminated thus making possible a completely fluid recording system.

The authors wish to thank the Bristol Instrument Company of Waterbury, Conn. for their cooperation in making the development of this cystometer possible.

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REFERENCES

Landes, H. E. and Voris, H. C.: J. Urol., **43:** 345, 1940.
Lewis, L. G.: J. Urol., **41:** 638, 1939.
Rose, D. K.: J. Urol., **17:** 487, 1927.
Rose, D. K.: J. Urol., **43:** 718, 1940.

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ADENOMATOID TUMOR OF EPIDIDYMIS

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Tumors of the epididymis are uncommon. Though cases have been reported, the number is so small that no satisfactory classification is available. More recently the term "adenomatoid tumor of the epididymis" has been used to group certain tumors exhibiting similar clinical and histopathological manifestations. There is some controversy regarding the etiology of such "adenomatoid" tumors. Most authors believe they are neoplastic, but of a low order of malignancy. In the case presented histologic evidence of an inflammatory reaction was present; although, otherwise, the lesion showed the classical features of the so-called "adenomatoid" group.

CASE REPORT

A 38 year old Negro mail-carrier was first seen in the dermatology clinic, complaining of a generalized skin eruption of 4 months' duration. Examination revealed skin lesions characteristic of secondary lues and the serological studies were confirmatory. The examiner also noted a "painless, hard right epididymis" which the patient had not known was present. Treatment consisted of 6,000,000 units of penicillin. Two months later the patient returned for re-examination and serological study, and at that time stated that for 3 days preceding he had had pain in the right groin, and that the previously painless nodule in the right epididymis was "tender," but the nodule had not increased in size. He was referred to urology clinic with the diagnosis of "acute right epididymitis."

The patient had had acute specific urethritis in 1939, treated adequately with sulfonamides. He denied having epididymitis by name or symptom then or at any time previously. There was no history of trauma to the scrotum or perineal region. He had no chronic urethral discharge, and had never been treated for "prostatitis."

The essential physical finding was a 1.5 by 1 by 1 cm., round, hard mass lying between the caput major of the right epididymis and the superior portion of the body of the right testis, and firmly attached to both. The mass was slightly tender to palpation, causing radiation of pain toward the right hip. There was no lymphadenopathy. Miscroscopic examination of prostatic expressate was within normal limits. Skin lesions recognized as the stigmata of secondary lues were still present.

The centrifuged urine contained 8–10 white blood cells per high power field. The red cell count was 3.83 million and the white cell count was 10,200 with normal differential, hemoglobin 11.8 gm. The chest film was normal. Complement fixation was 1 plus and the cardiolipin was positive. Prolan determination on a 12 hour collection of urine showed "hyperemia of ovaries and tubes, and

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Sponsored by the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are a result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

marked hypertrophy of ovaries, tubes, and uterus." The test animal was the white mouse, and only one such determination was made preoperatively.

A provisional diagnosis of "carcinoma of the right testicle" was made. Exploration of the testis and possible orchiectomy and retroperitoneal exploration were advised. At surgery the right testis and epididymis were exposed through a scrotal incision. A 1 cm., round, yellow-white, very hard tumor mass was found lying between, firmly fixed to, and infiltrating the caput major of the epididymis and the superior pole of the testis. The diagnosis was thought to be evident. The testis and epididymis were immediately excised, following which the right spermatic cord was removed to the hilum of the kidney through a retroperitoneal dissection. No evidence of metastatic neoplasm was found.

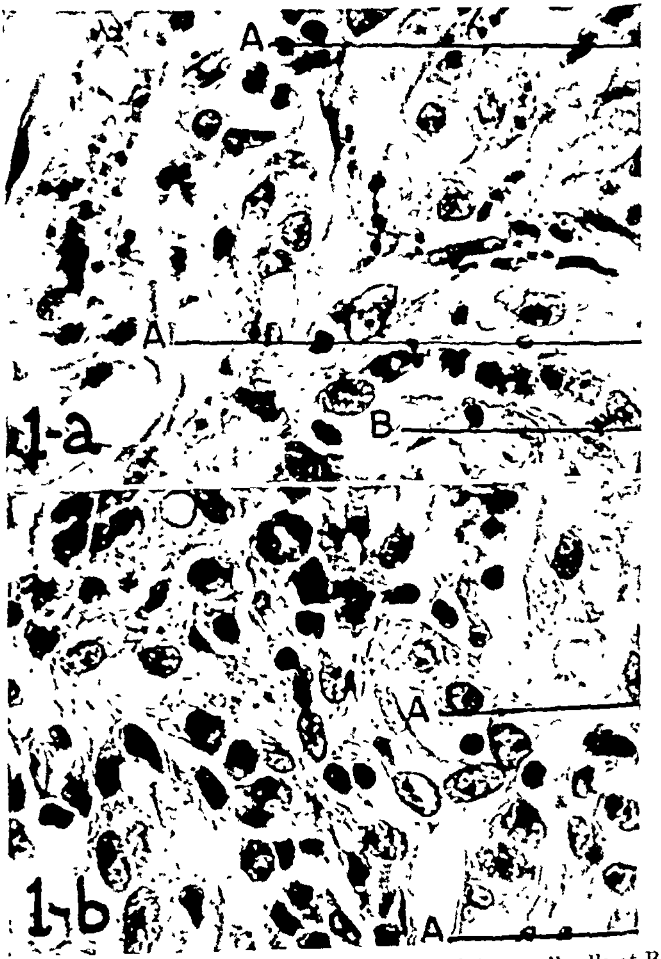

FIG 1 *1, a*, Note scattered leukocytes at A, and size of "tumor" cells at B Note cystic or vacuolated appearance of "tumor" *1, b*, Area showing numerous plasma cells in interstitial tissue. Note gland-like structures at A and vacuolated appearance of cytoplasm of some cells.

The postoperative course was smooth, the patient being ambulatory from the first postoperative day. He has returned to the hospital for post-surgical checkup, and the present time, three months following operation, is well and at work.

DISCUSSION

Tumors of the epididymis and the testicular tunics have been described for a number of years under a variety of names, depending upon the authors' concept as to their origin. Thus such tumors are classified as mesothelioma[1] lymphangioma and leiomyoma[2] or adenocarcinoma.[3] Others have believed that they are not neoplastic at all, but represent stages of chronic inflammation.[4] In 1945, Golden and Ash reviewed 15 cases and proposed the indefinite term "adenomatoid tumors", since they felt that the genesis of the tumors was obscure.[5] However, they definitely classified them as neoplastic.

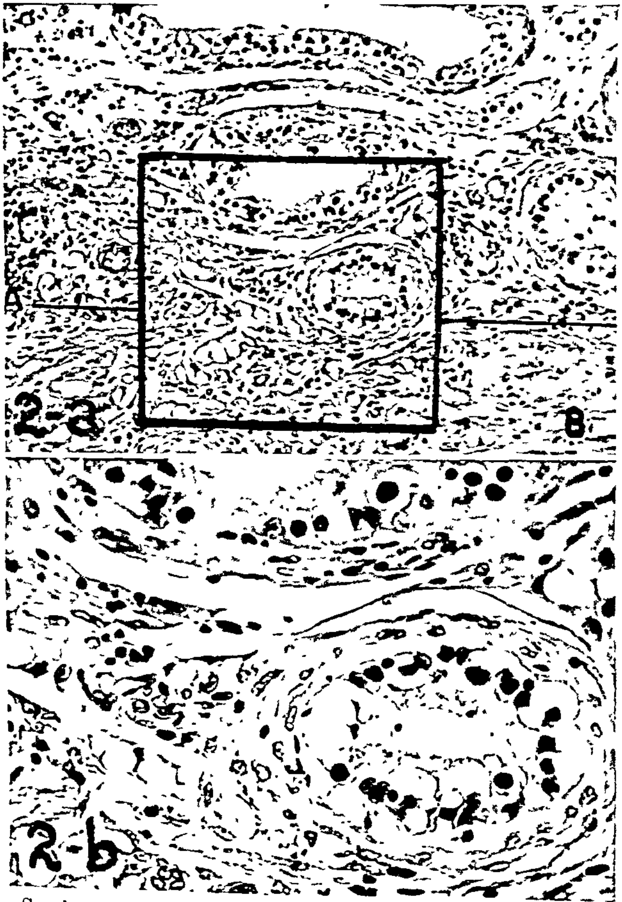

FIG. 2. *2, a.* Section of testicle and tumor. Note infiltration by "tumor" into testicle. Collection of lymphocytes is seen at A. Note atrophied seminiferous tubules at B. Higher power of outlined area is shown in *2, b*. *2, b,* Higher power of section outlined in *2, a*. Lower half of section shows usual vacuolated "sieve" like appearance of "adenomatoid tumors. Note degenerative changes in tubules in upper half of section.

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[1] Evans, N.: Mesotheliomas of the epididymis and tunica vaginalis. J. Urol., **50**: 249–254, 1943.

[2] Halpert, B.: Mixed leiomyoma and lymphangioma. J. Urol., **45**: 536–538, 1941.

[3] Thompson, G. J.: Tumors of spermatic cord, epididymis, and testicular tunics. Surg. Gynec. and Obst., **62**: 712–728, 1936.

[4] Mark, A.: Quoted by Golden and Ash.

[5] Golden, A. and Ash, J. E.: Am. J. Path., **21**: 63–80, 1945.

In the case presented the neoplastic nature of the tumor nodule was open to question; although, in general, the microscopic appearance of the tumor fitted into the group of adenomatoid tumors as described by Golden and Ash.[5] However, there were significant differences. Thus, the latter authors state: "The interstitial tissue contained a scattering of lymphocytes with an occasional admixed monocyte. Plasma cells, eosinophils, and neutrophils were absent. There was no evidence of the effects of chronic inflammation, such as scarring, adjacent to the lymphocytic foci. In none of the sections studied was there any evidence of invasion of the regional tissues. *Microscopically, the tumors could be shown to be either sharply circumscribed or encapsulated.*" In contrast to this description, the microscopic findings in the case here reported showed areas of necrosis, along the edges of which were numerous polymorphonuclear leukocytes, including eosinophils (fig. 1). Furthermore, instead of being sharply circumscribed, the lesion extended among and surrounded some of the seminiferous tubules (fig. 2) and it was not uncommon to find plasma cells in such areas. On the other hand, the histologic picture otherwise reproduced rather faithfully the findings of "adenomatoid tumor." Thus, there was a prominent fibrous supporting stroma throughout which were small groups, cords, or gland-like collections of "tumor" cells. These cells were quite large, measuring about 3 or 4 times the size of a red blood cell; the nuclei were oval with definite nuclear membranes, a lacy chromatin and one or two nucleoli. In many cells a striking *vacuolization was seen not only in the cytoplasm but also in the nuclei* (fig. 2, *B*). Even the stroma was vacuolated so that it had a sieve-like appearance. In some areas the cells were arranged around such a vacuolated space and thus resembled gland formation. Special stains for mucin were negative, but fat stains with Sharlach R showed small amounts of fat. Because of all of the above findings, the writers question the neoplastic nature of the "tumors." It is significant to note that these "tumors" have not been known to metastasize. It is of interest in this case that a positive gonadotropin was obtained on a mouse. However, only one mouse was used and no repeat test was done. Golden and Ash *refer to a similar result in one of the reported cases.*[5]

SUMMARY AND CONCLUSIONS

The clinical history and pathology of a case of tumor of the epididymis is presented and discussed. Though the tumor fits into the group classified as "adenomatoid" tumors, we believe that this tumor is inflammatory rather than neoplastic in origin.

Orchiectomy, though not indicated, was justified. It was impossible at surgery to differentiate the lesion from the malignant testicular tumors. There is controversy as to the exact nature of the lesion, even from prepared microscopic sections.[6]

1730 D St., Bakersfield, Calif.

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[6] Slides of this tumor were presented to the Tumor Slide Conference of the California Cancer Commission, held in Los Angeles on May 7, 1949. The greater number of examiners, including Dr. Nathan C. Foote, diagnosed the specimen as "adenomatoid tumor of the epididymis." Others, however, considered the lesion to be inflammatory in origin.

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AGENESIS OF ABDOMINAL MUSCULATURE ASSOCIATED WITH GENITO-URINARY AND GASTRO-INTESTINAL TRACT ANOMALIES

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Congenital absence of muscles of the anterior abdominal wall is a rare anomaly. Observations recorded in the medical literature would seem to indicate that any of the skeletal muscles may be congenitally absent;[1] however, none of them appear to be so consistently associated with other serious anomalies as when the abdominal muscles are absent. Obrinsky[2] (1949) was able to find 41 cases, and reported an additional one in which there was a combination of agenesis of the abdominal muscles and serious malformations of the genito-urinary tract. These malformations included an enlarged and hypertonic bladder, usually occupying an abdominal or fetal position, hydro-ureters, destruction or cystic degeneration of the renal parenchyma with dilatation of the renal pelves and calyces, and cryptorchism. Silverman and Huang[3] (1950) included 3 additional cases in their more recent review and reported 3 cases of their own, stressing the frequency of alimentary tract anomalies as well as the already recognized genito-urinary tract anomalies. The apparent recent interest in this syndrome would seem to justify this documented case to stress the prognostic significance of finding absence of abdominal muscles on the initial examination of a new born infant.

CASE REPORT

A full-term white male infant was admitted to the newborn nursery after birth. The mother of the infant was a 31-year-old gravida 4, para 2, who had had an uncomplicated pregnancy except for mild, recurrent edema of feet, ankles, hands, forearms and face which cleared on a salt-free diet. Her urine remained negative for albumin throughout the pregnancy, and her blood pressure was always within normal limits. She and her husband were Rh negative and she developed no Rh antibodies during this pregnancy. Her cardiolipin microflocculation was negative. The patient was delivered after a normal labor under gas-oxygen-ether anesthesia with low forceps and median episiotomy. Her third pregnancy had miscarried at 4 months of unknown cause and there were two normal living children, 4½ and 5½ years of age. The father was living and well. There was no history of familial disease or congenital malformation obtainable in other members of the family trees.

The infant breathed spontaneously after birth, was not cyanotic, and his general condition appeared to be good. His birth weight was 7 pounds, 2 ounces; length, 20 inches; occipitofrontal measurement, 14 inches; and chest, 13 inches. The eyes, ears, nose, mouth, and head appeared normal. There were no abnormal lung or heart findings. The skin over the abdomen, although intact, was remarkably wrinkled and redundant, and on palpation lacked tone or resistance, permitting palpation of virtually all abdominal contents. Two distinct rounded masses, approximately 1½ inches in diameter, which appeared to be cystic could be felt in the suprapubic region and left lower quadrant. Firm pressure on these masses resulted in the flow of urine through the urethra. The penis was extremely small and the testes were not in the scrotum. The spine and rectum appeared normal. There was a persistent inversion and varus deformity of the forefoot bilaterally, more marked on the left. There was a piston action of the left lower extremity at the hip joint and limitation of abduction of left hip with the thigh flexed to 90 degrees to the trunk. The level of the left knee was lower than the right when the thighs were flexed at 90 degrees.

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[1] Textbook Pediatrics: Mitchell-Nelson. Philadelphia and London: W. B. Saunders Co., 1950, 5th ed., p. 1489.

[2] Obrinsky, W.: Am. J. Dis. of Child. 77: 362, 1949.

[3] Silverman, F. N. and Huang, N.: Am. J. Dis. of Child., 80: 91, 1950.

Cord blood cardiolipin microflocculation was negative. Urine showed a trace of albumin, was negative for sugar, and negative on microscopic examination. Blood Rh was negative. X-rays taken 4 hours after birth showed evidence of dislocation of left hip, but no other bony defects in the entire skeleton. The lungs appeared incompletely expanded, but there was no evidence of diaphragmatic hernia. The urea nitrogen on the seventh day was 47 mg. per cent. A postmortem blood culture was negative.

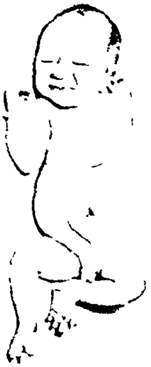

FIG. 1. Appearance of abdominal wall during first day of life

The infant voided and passed meconium stools normally. The pelvic masses disappeared after voiding. He took glucose water and then formula at regular intervals well, but lost 11 ounces during the first 5 days when his weight stabilized. During feedings on the sixth day jerky movements of the arms were reported, but no definite convulsion was observed and no positive evidence of neurological disease could be found on examination. On the seventh day 1½ ounce feedings were taken only with some urging. In the evening of the seventh day, 5 minutes after having been examined by the doctor and appearing unchanged, he was found very cyanotic and all vital signs were absent. He failed to respond to stimulants.

Clinical impression: 1) Agenesis of abdominal musculature with multiple anomalies of the genito-urinary tract; 2) uremia; 3) dislocation of left hip.

On opening the body there was a moderate amount of fetal, lobulated, subcutaneous fat. There appeared to be only thin strands of rectus muscle on the left and no demonstrable muscle within the right abdominal wall. The liver appeared large. The large intestine was only partially rotated, having descended to approximately half its usual position on the right. There was no evidence of gastrointestinal abnormality otherwise. There were two *intra-abdominal testes*, one in the right lower fossa and another in the left internal ring. The bladder appeared large with a thin-walled diverticulum, measuring 1 cm. at its base, in the dome. There was a cystic mass apparently connected to the bladder and ureter in the left lower quadrant, and another slightly smaller cystic mass apparently connecting with the right ureter lying posterior to the bladder. The proximal ureters appeared of normal caliber, but became tortuous before connecting with these two cystic masses. The kidneys were normally situated, but appeared very small in size, the right being smaller than the left. On individual examinations of the liver, spleen, stomach, intestine, pancreas, lungs, heart, and adrenals there were no additional abnormalities. The kidneys measured 1.5 cm. between poles. There was very little differentiation into cortex and medulla. There was no dilatation of the pelvis. There were several 4 mm. cysts near the periphery of the right kidney. Both ureters ended in the aforementioned cystic masses, which appeared to represent dilatation of the ureters in their distal portion. The ureteral orifices of the bladder appeared normally patent and admitted a probe into the dilated ureters. The proximal ureters were patent and of normal caliber. The bladder wall appeared thickened and measured 4 mm. There was no apparent obstruction at the bladder neck and the urethra was normally patent in the penis, permitting free expression of urine. See figure 2.

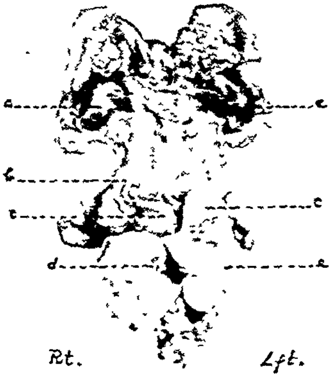

FIG. 2 To show urinary tract: *a*. Kidney; *b*, proximal ureter; *c*, dilated distal ureter; *d*, ureteral orifice; and *e*, bladder wall.

Microscopic examination of sections from the lung showed evidence of lanugo hair and desquamated epithelium in some of the alveolar spaces with little emphysema in the periphery of the lungs. Many of the kidney glomeruli were dilated to cystic proportions, others contained hyaline material and appeared fibrosed. The cortical glomerular-bearing area was considerably thinned. In one pole of the kidney there were aggregations of young squamous cells. The vessels in this kidney showed rather marked medial thickening. The mucous membrane of the bladder was of transitional type and overlay a normal submucosa and muscularis. There was abrupt thinning of the muscularis with apparent absence toward the center of an area representing the diverticulum on the dome of the bladder. Other sections were not significantly changed.

Anatomical diagnoses: 1) Agenesis of abdominal muscles; 2) agenesis of kidneys; 3) dilatation of distal end of ureter, bilateral; 4) dilatation and hypertrophy of bladder with diverticulum in dome of bladder; 5) intra-abdominal testes; 6) incomplete midgut rotation; 7) the probable cause of death is uremia.

DISCUSSION

Since the earliest reports of this remarkable combination of congenital defects, pathogenesis has been the subject most discussed, resulting in a wide variety of theories being given for the anomalies of the two systems occurring together so consistently. The abdominal wall in these cases certainly gives the impression that there has been a prolonged distention of the abdominal cavity which for some reason no longer exists, leaving the wall collapsed as in the abdomen of a mother following delivery (fig. 1). This appearance gave rise to the theory that the genito-urinary tract malformation is primary, resulting in prolonged distention of the bladder with secondary changes in the abdominal muscles by either dystrophy or atrophy. This concept seems untenable; first, because the abdominal muscles are formed by the end of the ninth week of fetal life, long before pressure can be exerted on them by distention of the urinary bladder;[3] secondly, urethral obstruction has been a rare finding in these cases; and thirdly, the familiar picture of obstructive uropathy in infants is not associated with absence of the abdominal muscles.[4] Others have advanced the theory that the primary defect is muscular and that the genito-urinary changes are secondary. Bardeen, in discussing Osler's[5] case, stated that it is possible that the lack of resistance normally met with in the abdominal wall by the bladder at the time the kidneys begin to secrete urine may cause the bladder to expand rather than to empty secretions into the amniotic cavity through the urethra. This mechanism hardly explains those cases showing other changes than dilatation of the urinary bladder. With our present scant knowledge concerning the exact relationship of one system to another in embryogenic growth and development, a more satisfactory suggestion is that of Silverman,[3] that during the sixth and seventh week of fetal life the muscular and urogenital systems are in the stage of development which, if arrested or altered, could produce the malformations described. Likewise the process of midgut rotation occurring between the fifth to tenth week of fetal life might give some clue to the frequency of anomalies of rotation occurring with this syndrome. Our case, as well as 9 out of 26 examined[3] either by autopsy or roentgenographically, showed anomalies of midgut rotation. It is therefore suggested that a disturbance in embryogenesis before the tenth week might result in the

[4] Campbell, M.: Pediatric Urology, with a section on Bright's Disease in Infancy and Childhood. New York: the Macmillan Company, 1937, vol. 1, p. 122.

[5] Osler, W.: Bull. Johns Hopkins Hospital, **12**: 331, 1901.

independent occurrence of these three system anomalies. There appears to be no case of the syndrome reported in the female. The two females in Silverman's[3] review probably should not be included since one of them obviously represented a massive omphalocele and there was no evidence of associated genito-urinary tract anomaly in the second. Occurrence only in the male is probably a significant observation, but the reason for it will also have to await a better understanding of human embryogenesis.

The survival rate is very low, with 60 per cent dying in early infancy. Those dying early undoubtedly represent cases with the more severe genito-urinary tract anomalies. The other reported cases are incapacitated more or less depending apparently on the severity of the genito-urinary tract anomalies.

Treatment would appear to consist of control of infection in the genito-urinary tract and surgical relief of obstruction when possible. Daut[6] reported one of the few cases in which obstruction of the bladder neck seemed to be contributing to the urinary difficulties. Surgical resection of the vesical neck in this case was followed by marked symptomatic improvement as well as a reduction in the severity of the urinary tract infection.

SUMMARY

An additional case with autopsy findings of agenesis of abdominal musculature associated with genito-urinary and gastro-intestinal tract anomalies is reported.

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[6] Daut, R. V., Emmett, J. L. and Kennedy, R. L. J.: Proc. Staff Meet., Mayo Clinic, 22: 8, 1947.

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THE LOGIC OF ANTIMICROBIAL THERAPY

RUSSELL D. HERROLD

From the Department of Surgery (Urology), University of Illinois College of Medicine, Chicago

It is indeed an honor in this capacity to address you, the largest Section of the American Urological Association. During the past 6 years, I have seen at close range the fine cooperation and spirit of the members in this society. Time does not permit the personal citation that many deserve, but I feel obligated to commend the members who have served on the Executive Committee. At the sacrifice of their time and at their own expense, they have attended consistently the important interim meetings of the Executive Committee. I can say this without personal inhibition, since all such meetings were held in Chicago and without sacrifice on my part.

No one, I believe, would attempt an address on such an occasion as this without considerable forethought. Due consideration was given other topics in medical urology, but I finally decided on the one that has been of great interest to me throughout the years, and from a therapeutic angle, particularly, since the advent of the sulfonamides. A part of my message is concerned with the demonstration of a method for antibiotic sensitivity tests that is simple, rapid, inexpensive and we believe astonishingly accurate. Its implications will be discussed and a brief review given of clinical observations during the past year.

Several months ago the Lederle Laboratories made available aureomycin test tablets with instructions in regard to their use in sensitivity tests. Reference was made to some work done by Bondi and his co-workers.[1] In comparing these prepared tablets with the regular crystalline aureomycin as available for oral therapy, it seemed to me that the latter was superior. In addition, since none of the other antibiotics were available in such a test tablet, it seemed more practical to use the undiluted powder of aureomycin to compare with the other undiluted antibiotics, terramycin, chloromycetin, penicillin and streptomycin.* It was found, however, that the regular penicillin G-potassium did not have enough body and was too soluble; further, it was found that the preparation of procaine G-300,000 units with 100,000 units of penicillin G-potassium was very satisfactory.

I have prepared some lantern slides which are almost self-explanatory, together with a brief history of each patient whose bacteria were submitted to the sensitivity test.

Slide 1: This slide concerns the ABST test on the urine of a male patient with

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I am indebted to Parke Davis and Company and the Lederle Laboratories for a generous supply of chloromycetin and aureomycin, respectively.

Presidential address read at annual meeting, North Central Section, American Urological Association, Milwaukee, Wis , October 11, 1950.

[1] Bondi, A. Jr., Spaulding, E. T., Smith, D. E. and Dietz, C. C.: Am. J. M. Sc , **213**: 221, 1947.

*Since this paper was written, sensitivity tablets of the other antibiotics have become available.

chronic prostatitis and cystitis of many months' duration. He had been given aureomycin prior to my examination. The Proteus bacillus was isolated, and a combination of chloromycetin and dihydrostreptomycin was given, and the Proteus bacillus was eradicated.

Slide 2: ABST method.

Simple—no dilution antibiotic necessary
Rapid—overnight reading in many instances
Inexpensive—saving of material and labor
Accurate—in vitro and in vivo correlate
Less chance of antibiotic deterioration

Slide 3: Antibiotic sensitivity tests.

ABST abbreviations
Aureomycin—A
Terramycin—T
Chloromycetin—C
Dihydrostreptomycin—DSM
Penicillin—P

Slide 4: Rating of ABST.

A—greatest inhibition
B—intermediate inhibition
C—very little inhibition
F—failure, or no inhibition

Slide 5: This is a direct inoculation of urine from a male patient with chronic pyelocystitis due to E. coli intermediate. A comparison was made of small and large deposits of dihydrostreptomycin with a difference of at least 20-fold and you will note that there is very little if any difference in the clear zone of inhibition of bacterial growth. Also in a like manner, small and large deposits of chloromycetin were made with similar results. The important thing about seeding of these plates is that the bacterial population should be sufficiently high so that there will be resultant heavy growth for relative comparison of inhibition of the various antibiotics.

Slide 6: This is urine from the same patient as illustrated in slide 5, but in addition to the antibiotics in the 4 corners, penicillin was deposited in the center of the plate, and you will note that it produces a zone of inhibition which will be discussed later. Now, however, we have found it was more practical to make the penicillin tests on a separate plate from the other antibiotics.

Slide 7: This slide illustrates the result of ABST tests on the urine from a female patient with a chronic infection due to mucoid E. coli, to whom aureomycin had previously been administered, and you will note that tests indicate the inhibition is less by aureomycin as compared to terramycetin, dihydrostreptomycin and chloromycetin.

Slide 8: This slide shows urine from a male patient in whom the infecting organism was Aerogenes. The patient had been given aureomycin several weeks prior to the ABST test and you will again note that it has the smallest zone of inhibition.

Slide 9: This is the case of a male patient with an acute prostatocystitis due to Staphylococcus albus. You will note that there is comparatively little difference in the four antibiotics tested, except that streptomycin appears slightly less effective, but test made on a separate plate indicated that penicillin was superior to the other four antibiotics. Penicillin was then administered to the patient and a clinical and bacteriologic cure obtained.

Proteose No. 3 agar or one with a slight variation of this formula with 1.5 per cent agar, was poured in the usual manner, with 25 cc to a Petri dish. After remaining at room temperature for 24 hours they were marked off into four quarters, and the urine to be tested was inoculated heavily and equally by means of a sterile swab. Aureomycin, terramycin, chloromycetin and streptomycin were each deposited at the border of each quarter, respectively, and at the outer border, midway between the dividing lines. The test plates were then placed in the ice box for 1 hour, after which they were incubated overnight. Thus, 4 specimens could be tested against these 4 antibiotics on four plates. A separate plate was used for penicillin with each quarter inoculated with the four different specimens. Penicillin was deposited on each of the four quarters in the same manner as with the other antibiotics. A control plate like that of penicillin was also made with seeding of the four separate quarters. It was found that there was considerable leeway as regards the amount of deposit. When it was increased 20-fold, or more, there was very little difference in the tests, indicating that dissemination through the medium was essentially the same with small as with large deposits. Generally, it was necessary that the urines be grossly cloudy and contain a substantial population of bacteria so that the growth would be heavy and confluent and the contrast clear-cut. In urines that are glossly clear where it is suspected that the bacterial population is low, concentration can be done by centrifugation and the sediment of 10 cc suspended in about $\frac{1}{2}$ cc after pouring off the supernatant urine. It is interesting to note that in contrast to previous sensitivity tests whereby the antibiotic is incorporated in the medium, there is no lag period, in which growth may occur later in the primary zone of inhibition. After overnight incubation, each zone remains clear and without growth indefinitely. It is well known that when some antibiotics are incorporated in the medium, bacterial stasis may occur for periods up to 4 to 5 days, after which growth will emerge. During this period of stasis, there may be considerable depreciation of the antibiotic which is incorporated in the medium. For pure coccal infections, this method seems to work as well as with pure coliform infections. However, in mixed infections, a more accurate evaluation can be obtained by seeding the exudate or urine first onto solid medium and then subculturing the various species into broth or sterile urine after 24 hours' growth. Inoculations are made in a like manner to that of the original urine in single infections.

There has been a close correlation between the in vitro and in vivo observations in order to evaluate more accurately their significance. I can state, without qualification, that the test tube pattern of aureomycin, terramycin and dihydrostreptomycin is almost identical with the results to be expected in the urine or adjacent tissue. The variability of penicillin to inhibit various coliform organisms and their lack of correlation in the body, I believe is due to the rapid development of resistance by coliform bacteria to penicillin with both in vitro and in vivo. As regards chloromycetin, the problem becomes more complicated. By the previously described method, the zone of inhibition of the growth of Proteus is consistently superior to aureomycin and terramycin, and certainly clinical observations bear out the superiority of chloromycetin over aureomycin and terramycin for Proteus infections. When there is clinical failure of chloromycetin against other gram negative bacilli which have been isolated during or subsequent to treatment, there will not always be a complete absence, but rather a definite reduction of the zone of inhibition. It may well be that there is a slower development of resistance to chloromycetin as compared to aureomycin, terramycin and streptomycin so that there is a longer period of partial resistance to chloromycetin before attaining complete resistance.

As regards the best combination of two or more antibiotics for certain offending organisms, we hope that this method may shed some light on more logical combinations. It will entail more information on the exact concentration of each antibiotic in the various zones from the deposits of two or more, which work is now in progress. Combined antibiotics may exert their influence in one of three ways: additive, synergistic or antagonistic.

Slide 10: The principles of combined therapy.
Additive effect—or 2 plus 2 equals 4
Synergistic effect—or 2 plus 2 equals 8
Antagonistic effect—or 2 plus 2 equals 1 or 0

Slide 11: A suspension of a stock strain of Staphylococcus aureus was made in distilled water and submitted to the effect of penicillin alone, dihydrostreptomycin alone, and the two combined. It will be noted that the zone of inhibition was the least with dihydrostreptomycin, intermediate with the mixture, and greatest with penicillin. It is possible that there was a competitive dissemination into the medium when combined, rather than a true antagonistic effect.

Additive is of very little value and may lead to sensitivity reactions to two or more antibiotics instead of one and also might lead to fastness to two or more antibiotics instead of one. Synergistic action definitely would be of help in selected instances. It is obvious, however, that antagonistic could be very detrimental.

Jawetz[2] and his co-workers have stated that chloromycetin-penicillin mixtures are antagonistic as regards their effect on enterococci, but that streptomycin-penicillin mixtures are synergistic. Streptococcus fecalis is a sub-group of enterococci. We have seen clinical and laboratory evidence of benefit from combined administration of penicillin-streptomycin for certain streptococci previously resistant to penicillin alone.

There is ample evidence that chloromycetin and streptomycin is the best combination for pure Proteus infection if not streptomycin-fast. It may be that terramycin is a shade better than aureomycin to combine with streptomycin for Pseudomonas, possibly because as a newer drug the organisms may not have been subjected to its influence previously. In general, for coccal infections where penicillin alone has previously failed to accomplish cure, aureomycin combined with penicillin would seem to be first choice and possibly terramycin a close second, but either preferable to chloromycetin. The sensitivity tests are of considerable aid here in making the best choice of combined therapy.

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[2] Jawetz, E., Gunnison, J. B. and Coleman, V. R.: Science, **111**: 254, 1950.

What in general about the development of resistance of bacteria to the newer antibiotics? All of us, clinicians and bacteriologists alike, have long known that this phenomenon occurs with streptomycin. We know that it is not unusual for staphylococci to develop resistance to penicillin. We stated at the A.U.A. meeting in Los Angeles in May 1949, that resistance can develop to aureomycin and chloromycetin. We can say more convincingly now that in the absence of cure, resistance frequently follows to such an extent that the antibiotics become valueless, particularly aureomycin, terramycin and streptomycin. Such resistance also can occur with chloromycetin, but the in vitro tests suggest that when only partial, the administration of chloromycetin with another antibacterial agent may be worth while.

Aureomycin and terramycin are very similar in their antibacterial spectrum or zone and in many other ways basically similar. But resistance to one does not always follow resistance to the other. They are quite dissimilar in many respects from penicillin, streptomycin and chloromycetin, so that fundamentally the five available antibiotics fall into four groups.

Every one of you, I am sure, is interested in the best regimen or bacterial prophylaxis pre- and postoperatively. Several months ago, we chose a combination of penicillin and aureomycin for this purpose. I am indebted to Dr. Joseph Kiefer and Dr. Cornelius Vermeulen, at the Research and Educational Hospitals, and to Dr. Kiefer at St. Joseph's Hospital, for permission to make use of their surgical patients.

Slide 12: Bacterial prophylaxis for surgical procedures. Aureomycin 250 mg. q. 8 hr. 24 hrs. prior to surgery and during hospital stay, or for at least 10 days postoperatively. Repository penicillin 200–400,000 units daily, concurrently with aureomycin.

Total number TUR—20
Other prostatic surgery—6
Other G-U surgery—17

Aureomycin was administered in a dosage of 250 mg. every 8 hours, starting 24 hours before surgery and continuing in general during the hospital stay of the patient. This was combined with an injection daily of 300,000 to 400,000 units of a repository penicillin, starting also one day prior to surgery. Results as anticipated were not of great value in preventing infections in patients subjected to transurethral resection of the prostate. There would seem to be no question that some sort of antibacterial attack is worth while to prevent bacteremia and other sorts of postoperative complications, and the above combination was well tolerated in the dosage given and would seem as good as any. Terramycin could well be substituted for aureomycin, but the use of both would not seem good logic, since one might be needed later, if the post-transurethral infections do not clear up spontaneously after 4 months. Some have advocated the combination of penicillin and dihydrostreptomycin for prophylactic purposes, but the objection here is the risk of the emergence of streptomycin-fastness, and this drug may prove very useful later to combine with another antibiotic depending on the bacterial flora and their relative resistance. It is hoped that the new combined product of repository penicillin and streptomycin will not be used so indiscriminately that there will be mass emergence of streptomycin-resistant bacteria.

Since the advent of aureomycin, chloromycetin and terramycin, I have noted the emergence of more resistant bacteria after ordinary coliform and the assumedly specific etiologic organisms had been eradicated. The chief offenders to emerge were the Proteus bacillus, Pseudomonas, and occasionally yeast, none of which were isolated in the original cultures. I have found, however, that even in their presence, when the urine remains grossly clear and the patient is free of symptoms systemically and locally, these secondary organisms frequently will disappear spontaneously. Therefore, at the present time, I follow the policy of watchful waiting with cultures at intervals of 3 to 6 weeks rather than a repetition of antibiotic therapy. However, no instrumentation is done during this period without suitable prophylaxis. Likewise, where the original offending organisms of the common coliform type persist after antibiotic therapy, the above procedure is also applied.

Some observations made in the past year with which many of you may be familiar, I thought were interesting enough to relate. It has been found that aureomycin ointment is very effective in most instances of balano-posthitis associated with phimosis as so frequently is seen in elderly patients. Such effect is probably due to the application locally of the drug in higher concentration than can be obtained by parenteral administration. One patient on whom it was used for this purpose reported that following the favorable response of the balanoposthitis, there was a marked reduction of secretion of Tyson's glands which has been sustained without further regular application of aureomycin ointment. Another indication for the local application of aureomycin is a persistent discharge, where the source appears to be largely in the anterior urethra, and for instillation in the anterior posterior urethra in chronic total urethritis. Here I have found the solution of crystalline ophthalmic aureomycin preferable. This preparation is commonly used by ophthalmologists. Another observation I believe worthy of note is the use of ACTH to control the severe urticarial reaction following penicillin therapy, some of which are considerably delayed and occur after varying periods of time following discontinuance of therapy. I know of one instance recently where such reaction occurred 10 days after penicillin therapy and antihistamine drugs controlled the reaction partially for only a period of a couple of hours. The lesions completely disappeared after the institution of ACTH therapy. The ACTH was administered for a period of 1 week.

On my return to Chicago, we plan to use the laboratory of St. Joseph's Hospital as a proving ground to demonstrate that the method of sensitivity tests described today will be of value in the management of infections other than those of the urinary tract. This should increase the demand for such tests, and make it easier for you as urologists to obtain routinely such clinical pathological service.

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TUBERCULOSIS OF URINARY TRACT

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The treatment of tuberculosis of the urinary tract has become a most fascinating one, and especially for me, who had to deal with this problem for nearly 40 years. How well I remember the first years, when we were less well equipped (no pyelograms, imperfect instruments). How proud was one to have established the fact that a patient had unilateral tuberculosis: nephrectomy could save him. Only a few years ago, many a hot discussion was heard among surgeons and urologists, but in the end nephrectomy was recognized as a good remedy. But little thought was given to the fact, nowadays generally recognized, that tuberculosis of the kidney was part of a generalization of the disease in the human body. Notwithstanding that, we booked remarkable results: once the kidney was removed, sometimes the cystitis subsided more or less, even to complete recovery. It was no wonder that we tried to make a diagnosis as early as possible, because we were in fear of the complicating cystitis tuberculosa. The sooner we operated therefor, the more was the chance that the bladder could be kept free of tuberculosis.

That era I should like to name the Wildbolz era after that eminent Swiss urologist, who advocated this early nephrectomy, this "Frühoperation" and who had many followers. Sometimes the operation took place in so early a period of the infection, that only after a long search one could find the small tuberculous lesion in the kidney. But after some years we came to the conclusion that so many patients, even after a most successful operation, were not restored to health. Even Wildbolz in his monograph mentioned the fact that in a rather astonishing percentage there remained a certain morbidity after nephrectomy.

More recently Oppenheimer and Narins made a study of 106 patients after nephrectomy for unilateral tuberculosis: 15 developed genital or osseous tuberculosis, 17 had residual tuberculous cystitis, 17 had (later on?) tuberculosis of the remaining kidney. I cannot follow these authors in their conclusion that they will wait for a long followed series of cases with streptomycin before they will change their opinion, that cases of unilateral tuberculosis should be subjected to operation in every case.

Nesbit and Bohne stated, that although a fair chance of recovery existed in 1380 patients to be cured by nephrectomy, only 50 per cent were alive after 5 years and that even if in the supposed healthy kidney bacilli were found.

Semb came to the same conclusion: 50–60 per cent cure only even in very selected cases of unilateral tuberculosis. The persistence of tuberculosis of the bladder, genital-pulmonary and bone tuberculosis had their share in the appreciable morbidity after operation.

My own experience and that of so many others are more or less the same.

Read at annual meeting, American Urological Association, Washington, D. C., May 30, 1950.

antibiotic. Among the publications I will first mention those of Lattimer. His results were most encouraging: 235 patients were treated. The best results were

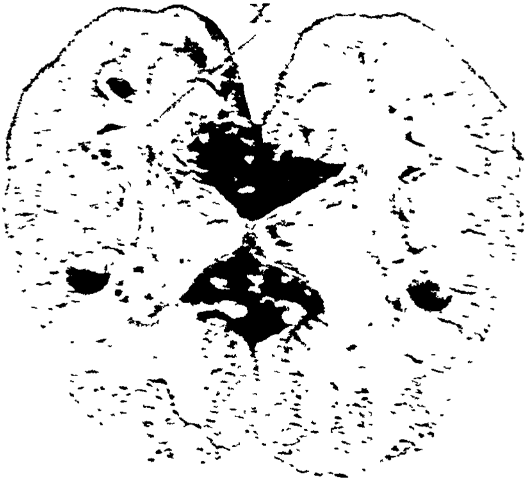

FIG. 1. X, drawn-up pyelum. Little is to be seen of tuberculous structure

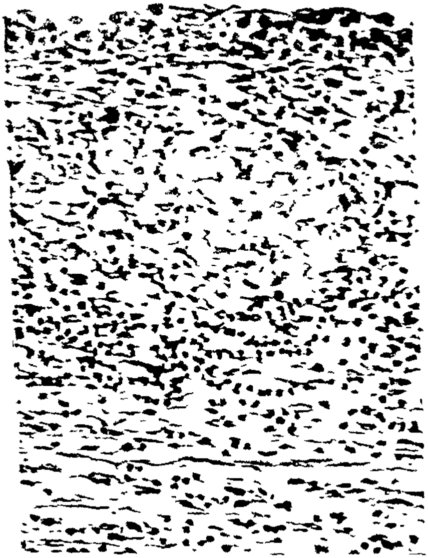

FIG. 2. Regressive epithelioid tubercle, just under mucous lining, seen in part of pyelum

obtained when streptomycin 2 gm. was given daily in 6 equal doses during 120 days. Most patients got vestibular symptoms, which in nearly all cases disappeared after the cure was ended. Streptomycin acts best in small unilateral

Therefore the fact remains that nephrectomy for unilateral tuberculosis of the kidney does not restore the patients to a healthy life, but there is a large percentage who are more or less suffering from various forms of tuberculosis.

In later years, Dos Santos of Lisbon and Bernard Fey of Paris opposed early nephrectomy. They were and are of the opinion that we should not operate as soon as possible after a diagnosis of unilateral tuberculosis. The idea is this: If the tuberculous kidney is still well functioning, they wait after careful examination of the case. If in months or years to come, the function becomes poor, then nephrectomy can be performed. The other kidney has been accustomed to do the work of the diseased kidney, and one is more sure of its condition. Examinations should be done at regular intervals. This point of view has at least the advantage that we do not operate in an acute phase of the tuberculosis, so that complications are to be feared much less. We could call this the era of delayed nephrectomy.

De Beaufond is of the opinion that the prognosis is not influenced by the fact when the operation is performed. His statistics of more than 550 cases show it. He gives support to Fey's *nephrectomie retardée*. De Beaufond had only 50 per cent of complete healing. Some of the bad results may be caused by the fact that we have to do with a generalization of the tuberculosis.

We all know Medlar's beautiful work, in which he established the fact that far more cases are bilateral than we know, and that even advanced cases, with tuberculous cavities in the kidneys had sometime no clinical symptoms.

We could easily fill a few pages with communications like these I mentioned above, but for our problem this is not necessary. It is clear that nephrectomy alone is not sufficient.

And now we come to the third era, which I should like to name after your world-famed countryman, the Waksman era. In this name I include the antibiotics and the drugs now in use and which give sometimes results, so astonishingly good, that our patients have got a new and more favorable outlook on life. I can only give you personal experience with 3 of them: streptomycin, PAS and moogrol.

Although I used vitamin D_2 and calcium in a few cases with no remarkable results, Stobbaerts' demonstration of a case, in which a small cavity was filled with a stone and the patient free of bacilli, made a very favorable impression.

Before I will speak about streptomycin and PAS, a few words about the use of chaulmoogra oil and its derivative esters, later on called moogrol. This oil should be able to dissolve the protective cell wall of the bacilli and make them more vulnerable for our new antibiotics and drugs. Slotkin in his publication gives a not convincing reproduction of the electronic micrograph magnification of Mycobacterium tuberculosis; but his successes in many cases treated with moogrol-streptomycin are most remarkable. And still more interesting is the publication of Duvergey: in a case of bilateral tuberculosis of the kidney. The bacilli disappeared definitely after treatment with chaulmoogra oil alone. I made it my practice to use moogrol in combination with streptomycin, (as Slotkin did).

And now I proceed with streptomycin and the results obtained with that antibiotic. Among the publications I will first mention those of Lattimer. His results were most encouraging: 235 patients were treated. The best results were obtained when streptomycin 2 gr. was given daily in 6 equal doses during 120 days. Most patients got vestibular symptoms, which in nearly all cases disappeared after the cure was ended. Streptomycin acts best in small unilateral

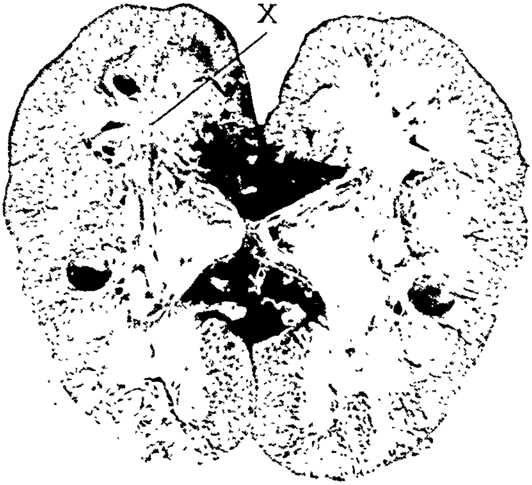

FIG. 1. *X*, drawn-up pyelum. Little is to be seen of tuberculous structure

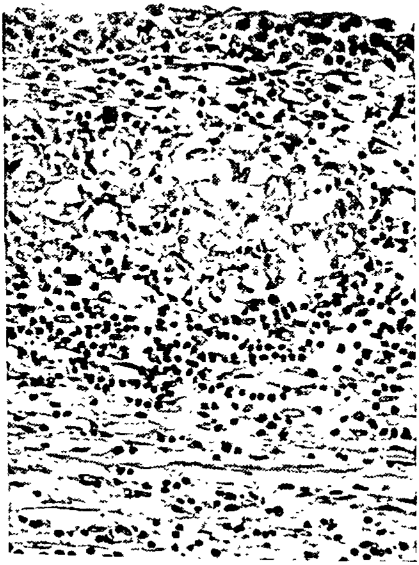

FIG. 2. Regressive epitheloid tubercle, just under mucous lining (cut in part of pyelum)

tuberculous alterations and when both kidneys produced bacilli without evident destruction in the pyelograms. In 80 per cent no bacilli could be found 12 months after the treatment.

Reed M. Nesbit reported 29 cases. His best results were obtained with streptomycin 2 gr. daily. If after 60 days there is no improvement, then operation. He keeps his patients in a sanatorium. Most of his patients got vestibular trouble.

Another potent drug against the bacilli which was discovered a few years ago is para amino salicylic acid (PAS). Now it is known that streptomycin given for a longer period makes the bacilli resistant against this antibiotic. Compared with streptomycin, PAS has the advantage that bacilli become resistant to PAS only after a longer period of treatment; streptomycin-resistant bacilli are susceptible to PAS; it enhances the action of streptomycin. It delays the emergence of streptomycin-resistant bacilli.

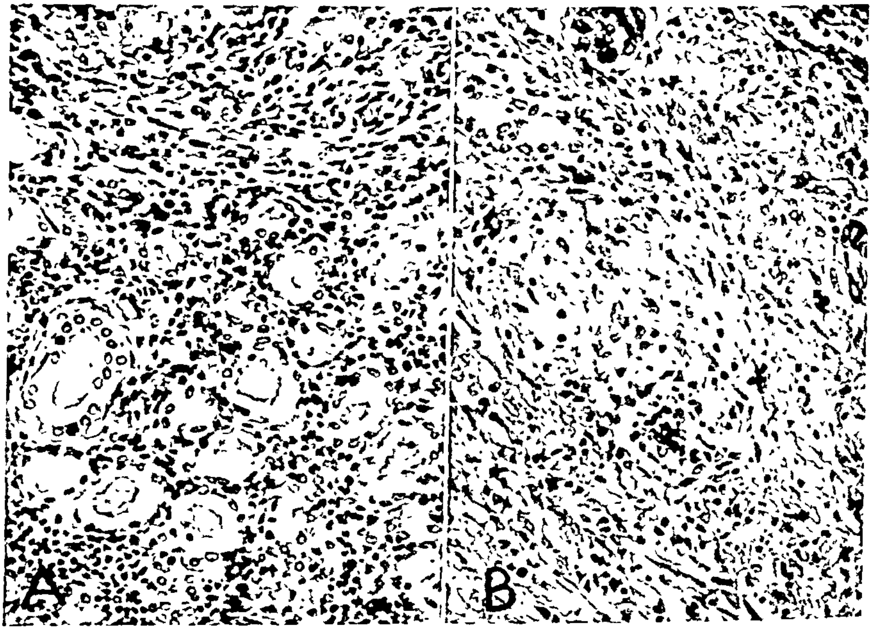

FIG. 3. *A*, cortex of kidney (in neighborhood of pyelum). Pseudothyroid structure as seen in chronic pyelonephritis. *B*, single fibrous tubercle in cortex near pyelum.

For these reasons streptomycin should always be combined with PAS. If we are obliged to operate upon a patient in a later period we must be very careful in administering streptomycin for longer than 6 weeks, for the patient will need the streptomycin after operation to avoid complications and the bacilli then must not have become resistent. The influence of PAS alone in a few patients, treated with it, was very promising.

My treatment nowadays is as follows: Urine should be made alkaline with sodium bicarbonate, then 1 gm. streptomycin, 12–16 gm. PAS or 20 gm. sodium PAS, 1 cc moogrol daily. I am well aware that I cannot give in detail my results. If I eliminate cases with complicating genital tuberculosis, I am very well satisfied with the results, although time since treatment is perhaps too short to speak of definite healing. In 7 cases with combined tuberculosis of bladder and single kidney (without cavities) after shorter or longer treatment, patients were free of symptoms; culture and guinea pigs became negative.

Of another case, I shall give a short summary: A girl aged 23 had tuberculosis of the knee and the twelfth rib. She was in Switzerland for a cure. In 1948 a urological examination disclosed that the urine was positive for tuberculosis. Destruction was present in the upper pole of the right kidney. Urine from the left kidney was positive. The patient was sent to me for a right nephrectomy after a cure with streptomycin and large doses of PAS. In August 1949, examination by me disclosed that urine from the left kidney and bladder was positive. But to my surprise, the right kidney no longer was tuberculous, as established by culture and guinea pig inoculation. After a cure of 1 month with streptomycin, PAS and moogrol, the urine was negative.

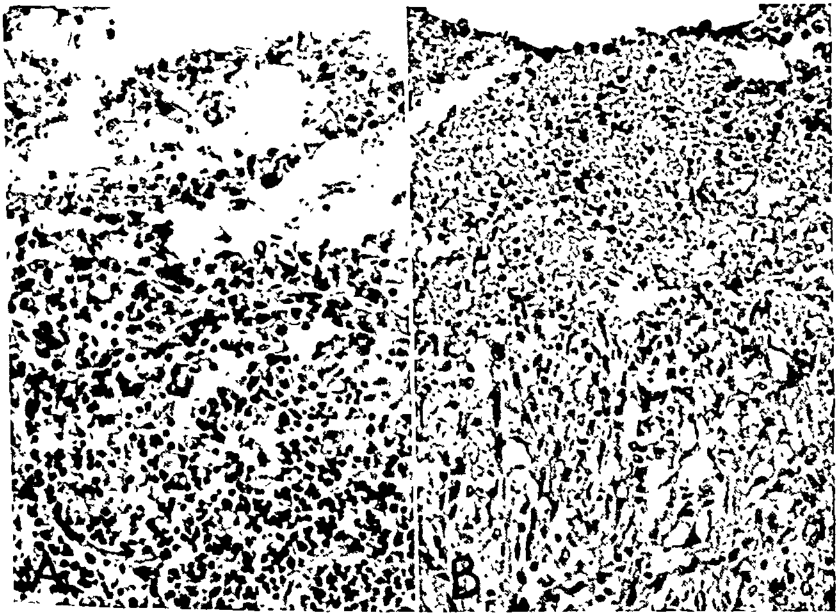

FIG. 4. *A*, wall of cavity covered by granulations. No necrosis, no tuberculous structure. This is part of tuberculous cavity, which we consider as healed. *B*, only in circumscript part of cavity we find wall covered with active tuberculous granulations and necrosis (fibroblasts in palisade stand).

Another case I should like to present ended with a nephrectomy, but a careful examination of this kidney shows clearly the healing power of streptomycin-moogrol. The patient was a man aged 42. He had tuberculosis of the right knee. Albumin, pus and bacilli in a density seldom seen appeared in the urine. Urography showed a small cavity in the right upper pole near the pyelum. The left kidney was normal. Streptomycin 1 gr. and moogrol 1 cc daily were given for 2 months, after which the urine became clear, with only a trace of albumin, a few pus cells, and with great difficulty one or two bacilli were found. I was inclined to continue treatment, but the patient and his family desired operation, which I performed with reluctance. Professor Deelman of the University of Amsterdam has examined this very precious piece with great care. He found a tuberculous process with every tendency to healing. I add some illustrations (figs. 1, 2, 3, and 4) to show you the details. It was a revelation for me to see a kidney which had produced purulent urine, with enormous quantities of bacilli, and where a cavity was on its way, to be cleansed.

Which in the end will be the best treatment remains to be seen. But in addition to the remedies, of utmost importance to bring all these patients to a cure is that they must be treated in a sanatorium.

REFERENCES

deBeaufond: 7th Congress of International Society of Urology, 1947.
Duvergey, H.: J. d'urol., **55:** 348, 1949.
Fey, B.: J. d'urol., **49:** 383, 1941.
Lattimer, J. K., Amberson, J. B. and Braham, S.: J. Urol., **62:** 875, 1949.
Medlar, E. M., Spain, D. M. and Holliday, R. W.: J. Urol., **61:** 1078, 1949.
Nesbit, R. M. and Bohne, A. W.: J.A.M.A., **138:** 927, 1948.
Oppenheimer, G. D. and Narins, L.: J. Urol., **62:** 804, 1949.
Semb, C.: Acta chir. Scandinav., **98:** 457, 1949.
Slotkin, G. E.: J. Urol., **58:** 464, 1947.

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DISCUSSION

DR. JOHN K. LATTIMER (New York, N. Y.): Our treatment of choice for bilateral renal tuberculosis is a combination of streptomycin and PAS, given together for one year. At our research unit for genito-urinary tuberculosis we give 12 gm. PAS by mouth and 1 gm. streptomycin, in one injection, each day. Like Dr. Van Cappellen we try never to give streptomycin alone any more, because if the combination is given, resistance to either drug is very slow to develop.

A tuberculous kidney should never be removed hastily. Dr. Van Cappellen has made an excellent point that, as is shown in these wax models, both kidneys of a tuberculous patient must be assumed to contain multiple small metastatic tubercles. Before we remove one kidney, we must be absolutely sure that the ureteral urine from the other kidney contains no tubercle bacilli or pus cells. If the active tuberculosis is bilateral, we give a year of treatment. Over the course of a year your patients will tell you that they become tired of PAS. Therefore, we vary the method of administration. We give it sometimes as tablets, not (3 gm. 4 times a day), or as powder stirred up in milk or fruit juice, or we can dissolve it in a bicarbonate solution, flavor it and give it as a liquid.

Your patients will also tell you that they have some softening of the bowel movements from PAS, and rarely, some distention. It is not severe. There is little or no nausea. These symptoms can be controlled easily by giving a little gelusil or amphojel before each dose of PAS.

Tuberculosis is much too chronic a disease, at least in our experience, to be stamped out by short courses of chemotherapy. You have seen our results in previous years with streptomycin alone, with 80 per cent conversions of the urine from positive to negative, dropping off to 60 per cent after a year or two, but in general holding up pretty well. Unfortunately, this requires a large dosage of 2 gm. of streptomycin per day, given for 4 months, and the patients become permanently ataxic. When we cut down the dosage or the length of treatment, we have had less satisfactory results.

We then tried combining streptomycin with promizole, but this drug was too toxic and we had to abandon it. When we first tried to combine streptomycin with PAS we had fine initial results but if we stopped the streptomycin after 6 weeks and kept the patients on PAS alone the results were unsatisfactory. The patients all became positive again. We think that this is evidence enough that the streptomycin is much more potent than the PAS.

Our results from long term combined treatment are not yet statistically significant due to too few cases or too short a follow-up, but when we gave the two drugs together for 90 days we got good initial results. These deteriorated badly as 6 months passed. We then tried a series with 4 months of streptomycin (1 gm. daily) and six months of PAS. The initial results were excellent but some of these patients are now beginning to show tubercle bacilli in the urine again.

In view of this experience we are now giving one year of streptomycin, and one year of PAS, in combination.

As to the newer drugs which you read about in the newspapers, Dr. Waksman's neomycin is still too toxic to be given parenterally. There is another excellent drug called mycomycin which is being developed but it is so unstable that you would have to keep not only the medicine but also the patient in the icebox. Streptomycin is apparently, from our experience, superior to dihydrostreptomycin, so we are using ordinary streptomycin. Then there is TB-1, which you have read about. This is the thiosemicarbazone which the Germans developed. We found it too toxic and are abandoning it in its present form. New, nontoxic derivatives may be developed. It is not quite as good as PAS. Other additional drugs are now being developed.

It is our opinion, in view of our experience with renal tuberculosis and with some pulmonary cases, that the best chemotherapy that is available to you as *of this moment is a combination of 1 gm. streptomycin, one injection per day, plus 12 gm. PAS, given by mouth; the combination to be given together for a period of one year.*

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RENAL TRAUMA: A STUDY OF 71 CASES

CLARENCE V. HODGES, DONALD R. GILBERT AND WILLIAM W. SCOTT

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Trauma to the kidney presents a critical situation which demands prompt, active management along preconceived lines.

Until fairly recent times, the majority of surgeons, both general and specialist, have held to the belief that these cases were best treated by expectancy and supportive measures until such time as the increasing gravity of the condition constituted a direct and immediate threat to life. Powers[1] stated that "the majority of patients with renal trauma may be treated conservatively with the expectation that the injured kidney will recover sufficient function to be a useful and serviceable organ." Priestley[2] held that "extensive urologic investigation, including cystoscopy and retrograde pyelography, immediately after renal injury is usually unnecessary and often undesirable" and that "in the majority of cases, medical treatment will be followed by functional results which are satisfactory, although various types of anatomic abnormalities may persist." He noted that, of 19 patients treated medically, 26.3 per cent still had symptoms referable to previous kidney injury, although these symptoms were not incapacitating. Sargent[3] was in favor of complete urologic study, including retrograde pyelography, to determine the extent of injury but in 1945[4] stated the principle that "most kidney injuries should be left alone. If the renal pelvis is reasonably intact the patient will soon recover. If the contour of the pelvis is blasted beyond recognition, nephrectomy is necessary." In support of the above views, it is conceded that urological experience includes many instances of slight or moderate injury to the kidney in which conservative therapy has resulted in a return to normal health.

In cases where the injury is more extensive, the policy of nonsurgical management has several major defects.

1) The period of "watchful waiting" may well extend beyond the optimal period for surgical intervention which usually occurs after the initial interval of shock has been overcome, thus prejudicing the patient's chances for survival. Cheetham[5] stated that the majority of operative deaths are due on the one hand to the severity of the primary injury, and on the other to procrastination in exploration. Swan,[6] citing 1,232 cases of renal injury treated by nonintervention, in which 264 (21.4 per cent) died, gave as his belief that "of this group many that

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All cases included in this series were seen at the Brady Urological Institute, Johns Hopkins Hospital, Baltimore, Maryland.

[1] Powers, J. H.: Surg., 3: 397, 1938.

[2] Priestley, J. T.: Surg. Clinics of N. Amer., 19: 1033, 1939.

[3] Sargent, J. C.: J.A.M.A., 115: 822, 1940.

[4] Idem: J. Urol., 53: 381, 1945.

[5] Cheetham, J. G.: Surg., Gynec. & Obst., 72: 573, 1941.

[6] Swan, R. H. J.: Brit. J. Urol., 12: 161, 1940.

died from hemorrhage might have been saved if timely operation had been performed."

2) Late complications, the sequelae of extravasation of blood and urine with subsequent infection, may arise. These include abscess formation,[7] hydronephrosis, pyonephrosis,[8] calcified hematomas and cyst formation,[9] pyelonephritis and secondary hypertension,[10] calculosis (*Lazarus*[11] *who cites one case and quotes* reports of Hinton, Torres, Masnata, Sabrozes and Bonnes, Kendall, Dubner, Rosen, Dozsa, Stirling and Lands, Livermore, and Volkmann—stone formation ascribed to antecedent trauma), and diminution or complete loss of renal function.

3) Unassociated renal disease,[6, 12, 13] underlying and contributing to the symptoms of kidney injury, may go unrecognized unless all diagnostic measures, including surgical exploration, are utilized.

4) Patients who are treated nonsurgically often undergo a protracted convalescence and remain "renal cripples" for weeks, months, or even years following their injuries.[8, 9, 14]

CLASSIFICATION

Hinman,[15] Ritvo and Stearns,[16] Stirling and Lands,[17] and Prather[18] have formulated classifications for renal injuries, based on clinical studies and experimental trauma in animals. While these are of value in retrospective analysis, the sum total of positive evidence gained by all diagnostic procedures, short of surgical exposure and visual examination of the kidney, is frequently too inconclusive to provide so detailed an estimate of the degree of injury. We have found a simpler, more condensed classification to be of practical value in determining the *indications for nonsurgical as opposed to surgical management.* In the majority of instances, a particular case will be found to fall into one of three definite categories: 1) minor injury (contusion); 2) major injury; 3) critical injury.

Minor injuries. Anatomically, such patients have suffered parenchymal damage without rupture of the capsule or extension of the defect into the pelvis or calyces. They do not usually exhibit shock unless there is more severe injury to other structures. Although hematuria may be alarming at first, it subsides to microscopic proportions within 48 to 72 hours. Pain, tenderness and splinting on the affected side may also be marked on first examination, but these symptoms, too, improve rapidly. No mass is palpable on physical examination of the kidney region (although it must be emphasized that splinting may conceal a mass of sizable proportions and that such a mass may be palpable only under general or spinal anesthesia). Most important, excretory and retrograde pyelograms show that the pelvis and calyceal system are intact on the injured side; the demonstration of their integrity constitutes the greatest single criterion for placing injuries in the minor group.

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[7] Turton, J. R. H.: Med. Press, **207**: 36, 1942.
[8] Robertson, J. P.: South. Med. J., **35**: 181, 1942.
[9] Colston, J. A. C. and Baker, W. W.: Arch. Surg., **34**: 99, 1937.
[10] Braasch, W. F. and Strom, G. W.: J. Urol., **50**: 543, 1943.
[11] Lazarus, J. A.: Urol. & Cutan. Rev., **43**: 529, 1939.
[12] Harrison, J. H.: Surg., Gynec. & Obst., **70**: 93, 1940.
[13] Jewett, H. J.: J. Urol., **43**: 664, 1940.
[14] Stearns, D. B.: Mil. Surg., **86**: 284, 1940.
[15] Hinman, Frank: Principles and Practice of Urology. Philadelphia: W. B. Saunders Co., 1936, p. 1009.
[16] Ritvo, Max and Stearns, D. B.: J.A.M.A., **109**: 1101, 1937.
[17] Stirling, W. C. and Lands, A. M.: J. Urol., **37**: 466, 1937.
[18] Prather, G. C.: J.A.M.A., **114**: 207, 1940.

Major injuries. Retrospective analysis of the group of cases which have been designated as "major" kidney injuries has shown that the anatomic lesion consists of parenchymal damage and capsular rupture with, almost invariably, extension of the disruption into the pelvis or calyces. While it is possible to achieve parenchymal damage and capsular rupture without perforation of the collecting system by means of the application of gradually increasing degrees of trauma to the exposed kidneys of experimental animals,[16] clinical experience indicates that injury severe enough to cause extensive parenchymal and capsular damage will usually result in perforation of the collecting system as well. Thus, a palpable perirenal hematoma is commonly accompanied by evidence of urinary extravasation on retrograde pyelography, the co-existence of the lesions being verified at operation by the presence of both blood and urine in the mass surrounding the injured kidney.

Patients who have suffered a major kidney injury present a diagnostic problem of marked proportions. Shock may or may not be present initially; its onset may be delayed for hours, days or even weeks following the traumatic incident.[19] Pain and splinting are usually present on the affected side, but may be obscured, at first examination, by symptoms and signs originating in trauma to other structures. Unlike minor renal injuries, however, the symptoms referable to the injured kidney tend to persist and to increase in magnitude. Hematuria is variable and may be inversely proportional to the degree of injury. A perirenal mass may be palpable only under anesthesia although it may occupy the entire renal fossa. We wish to strongly emphasize that physical examination may be entirely misleading in such cases. The use of the precise methods of diagnosis available to the urologist will do much to clarify the situation. The demonstration of extravasation on urography places the case directly in the "major" category.

Critical injuries. Extension of the disrupting lesion into the vessels of the renal pedicle constitutes the anatomic justification for placing injuries in the "critical" category. There is usually extensive pulpefaction of the renal capsule and parenchyma. The increasing mass in the exquisitely tender, splinted loin, along with early, profound shock and other evidences of massive hemorrhage, furnish sufficient clinical information to attest to the severity of the lesion. Excretory urography is of value chiefly in determining the presence and adequacy of the kidney on the uninjured side; it may yield valuable information even before shock has been thoroughly controlled. Retrograde pyelography is seldom necessary.

REPORT OF CASES

Seventy-one cases of renal injury were seen at the Brady Urological Institute from 1930 to 1948.* On the basis of the simplified classification which we have cited previously, the following incidence in each of the three important categories has been observed:

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* Permission to cite cases previously reported by Colston (6 cases), Jewett (1 case), and Wood (1 case), is gratefully acknowledged.

Total number of cases	71
Minor injuries	47 (66.2%)
Major injuries	23 (32 4%)
Critical injuries	1 (1 4%)

No mortality attributable to the renal injury has been encountered in this series.

A. *Minor injuries.* The right kidney was injured in 25 instances, the left in 22. Gross hematuria was observed in 29 cases, microscopic in 18. The average period of hospitalization was 8 days.

Urography: Excretory urography showed normal renal outlines and good function bilaterally in 25 (53.2 per cent) out of 47 cases. In 10 cases (21 per cent) excretory studies showed poor visualization or complete failure of excretion of the radio-opaque material; in these, retrograde studies of the injured side yielded the important information that there was no extravasation of dye, i e., the pelvis and calyces were intact. X-ray studies were not made in 12 cases; inclusion of these in the category of minor injuries has been, of necessity, based on the absence or rapid disappearance of symptoms.

The fact that 6 cases (12.8 per cent) were found to have severe, unassociated renal disease indicates that the pathologic kidney reacts to trauma to a degree out of proportion to the extent of the injury and constitutes a strong indication for thorough urologic investigation in every case encountered. The underlying lesions discovered were: 1) papillary carcinoma of renal pelvis; 2) "hypernephroma"; 3) unilateral fused kidneys; 4) congenital polycystic disease; 5) bilateral congenital hydronephrosis; 6) unilateral congenital hydronephrosis.

B. *Major injuries.* For purposes of analysis, the 23 cases of major injury to the kidney may be subdivided into 3 groups.

Group 1 (9 cases, 39 per cent): Major injuries seen soon after the traumatic incident in whom surgery, not dictated by life-saving considerations, was carried out to prevent major sequelae or to preserve renal function.

The average interval of time between injury and operation was 60 hours. In 5 cases (55 per cent of group 1), the injured kidney was repaired; 4 cases (45 per cent) were nephrectomized. The average period of hospitalization (corrected in one instance for multiple injuries to other systems) was 19.1 days.

Follow-up: Of the 5 instances in which early surgical repair of the kidney was carried out, 4 (80 per cent) exhibited no significant complications or sequelae attributable either to the injury or to operation over postoperative periods ranging from 4 months to 8 years. No follow-up was obtained on the fifth case. Of the 4 nephrectomized patients, 2 have shown no sequelae, and it may reasonably be assumed that the third, in whom no follow-up was obtained, had no further trouble, since the kidney was removed. The fourth nephrectomized patient (in whom carcinoma of the ureter was present at the time of surgery) died 2 years later of carcinomatosis.

Group 2 (3 cases, 13 per cent): Major injuries seen immediately after the traumatic incident in which surgery, although indicated by our present criteria, was not carried out.

The average period of hospitalization was 20 days. Inclusion in the category of major injuries is based on urographic evidence of extravasation in 2 cases; in the third, a perirenal mass developed during the period of hospitalization and urographic studies, carried out 4 months later, showed hydronephrosis and distortion of the calyces.

TABLE 1. *Major injuries treated initially by nonsurgical methods*

(Group 2) Major Injuries Seen Immediately After Trauma (Follow-up) (3 cases)

CASE	SEX	AGE	NATURE OF TRAUMA	POST-TRAUMA INTERVAL	SYMPTOMS	CONDITION	LATE OPERATION
1 (W. B.)	M	55	Crushing injury	7 years	None	No subsequent studies	None
2 (W. M.)	M	10	Fall	8 years	Extravasation on retrograde studies—could not be contacted for follow-up		
3 (A. H.)	M	23	Fall	4 months	None	Hydronephrosis	
				15 years	Occ. pain	Same (?)	None

(Group 3) Major Injuries Seen Late After Trauma (11 cases)

CASE	SEX	AGE	NATURE OF TRAUMA	POST-TRAUMA INTERVAL	SYMPTOMS	CONDITION	LATE OPERATION
4 (D. C.)	M	7	Fall	2 years	Pain	Hydronephrosis and nonfunction	Nephrectomy
5 (W. H.)	M	67	Fall	6 years	Renal colic, hematuria	Calculus and fibrolipomatous replacement	Nephrectomy
6 (T. H.)	M	9	Fall	10 weeks	None	Nonfunction	Deferred
7 (A. R.)	M	55	Boating accident, blow to side	6 years	Pain	Recurrent calculi, stricture of U-P junction	Nephrolithotomy (2) stricture dilated
8 (S. T.)	M	46	Severe blow left kidney	35 years	Pain	Calcified cyst	Partial removal of cyst
9 (L. M.)	M	27	Fall	15 years	Pain	Hydronephrosis calculi	Nephrectomy
10 (S. S.)	M	21	Sledding accident	21 years	Pressure, numbness of left leg	Renal cyst	Partial excision and marsupilization
11 (S.)	M	42	Automobile	1 month	Severe pain, hematuria and shock	Complete rupture	Nephrectomy
12 (W. M.)	F	47	Severe blow	3 years	Hematuria pain, urinary infection	Defect lower pole	Refused
13 (P. S.)	M	8	Fall	2 years	None	Nonfunction	Deferred
14 (E. L.)	M	8	Fall	21 days	Pain	Renal cyst	Removal of renal cyst

Follow-up: Of the 2 patients who showed urographic evidence of extravasation, one has had no further symptoms; the second could not be contacted. The third, in whom hydronephrosis was demonstrated 4 months following injury, has had occasional pain in the region of his injured kidney during the ensuing 15 years, but it has not been incapacitating.

Group 3 (11 cases, 48 per cent): Major injuries seen late after trauma.

Patients in this group were seen from 21 days to 35 years following the initial renal trauma. In 8 of the 11 cases, late surgery was necessitated by incapacitating sequelae which can reasonably be attributed to the original trauma. In the 3 remaining cases, surgery was either refused (1 case) or deferred, due to the asymptomatic status of non-functioning kidneys.

Groups 2 and 3 are summarized in table 1.

In considering the total of 14 patients with major injury who were treated by nonsurgical methods during the immediate post-injury period, it will be noted that 12 (85.7 per cent) have developed renal disease of severe proportions on the injured side. In the remaining 2 cases, the exact functional status of the injured kidneys is not known. In the absence of symptoms, we have elected, for purposes of this report, to consider them as having healed satisfactorily, but the fact that 2 other cases, also asymptomatic, show nonfunctioning kidneys on urography, casts some doubt on the validity of this assumption. In 8 of the 12 cases with proven severe sequelae, late surgery has been necessitated by incapacitating symptoms. In the remaining 4 cases, the necessity for surgical intervention remains a potent possibility.

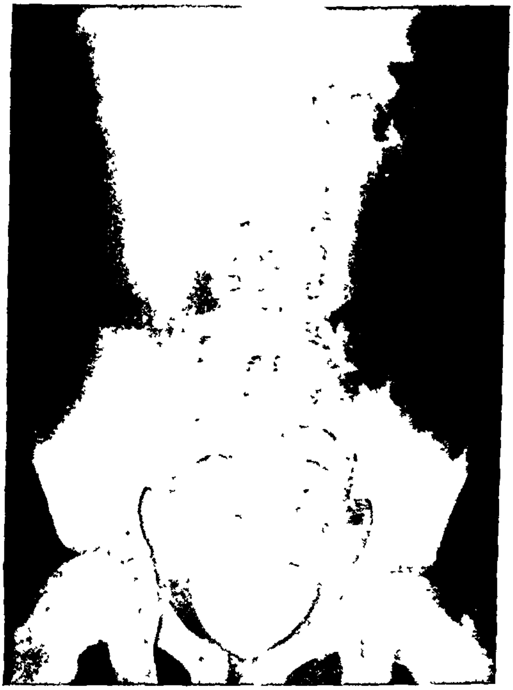

Fig. 1. Excretory urogram. Critical injury of right kidney

C. Critical injuries. One case falls in this classification.

An 11 year old white boy (T. K.), injured in a sledding accident, was brought to the hospital in severe shock on January 29, 1948. His voided urine was grossly bloody and contained clots. A tender mass occupied the entire upper right quadrant and loin. Whole blood 2,000 cc and the utilization of other standard supportive measures were necessary before the degree of shock was lessened. An excretory urogram (fig. 1) performed while the patient was in upper shock levels, showed normal configuration and excellent function on the left side. The right kidney outline could not be defined, and there was no evidence of function on this side; the characteristic "ground glass" appearance of a fluid-containing mass was noted in this area. After vigorous supportive therapy for 24 hours, the patient's blood pressure had risen to normal levels and the pulse rate decreased to 100 beats per minute. After what we now consider to have been an unpardonable delay of an additional 12 hours, the patient's condition showed general deterioration: falling blood pressure, rising pulse and an increase in the size of the perirenal mass. Operation, carried out 36 hours after injury, revealed a large amount of old and fresh blood in the perirenal space and extending down along the ureter. Alarming fresh hemorrhage, initiated after a portion of the hematoma had been evacuated and originating in a tear extending into the renal pedicle, was controlled by thrusting the fingers beneath the kidney and grasping the pedicle. Pedicle clamps were then applied and the severely damaged kidney removed. Convalescence was uneventful, the patient being discharged on the eleventh postoperative day.

DISCUSSION

We have emphasized the fact that physical and laboratory examinations are often insufficient for accurate determination of the degree of kidney injury. Moreover, it has become increasingly apparent in this study that excretory urography, while extremely valuable in demonstrating the presence of a normally functioning kidney on the opposite side, is frequently unsatisfactory in delineating the extent of injury on the affected side. Slight injury may result in complete suppression of function or in slight excretion of the radio-opaque material with disappointing lack of definition of the pelvis and calyceal structures (10 out of 35 cases of minor injury studied by excretory urography in this series); conversely, prompt concentration of the dye may occur in a kidney which has sustained considerable trauma. The latter situation is illustrated in the following case:

L. F., a 9 year old colored boy, was struck in the left side in a sledding accident 36 hours before admission on February 1, 1948. Severe initial pain in the left renal region gradually subsided during the following 24 hours, as did a bout of emesis. Hematuria was not noted. On admission, the patient was cooperative, rational and showed no evidence of marked distress. Blood pressure was 110/70; pulse 120. There was tenderness and marked muscle guarding over the entire left abdomen, flank and loin; no masses were felt. Laboratory examination showed no significant abnormality except microscopic hematuria. Excretory urography (fig. 2, *A*) on admission and 2 days later showed a normal right kidney. The left kidney, although its outline could not be made out satisfactorily, excreted dye promptly on each occasion. The upper major calyx was sharply defined; collections of dye in the regions of the other major calyces and the renal pelvis suggested distortion without evidence of extravasation; in other words, the findings on excretory urography were in keeping with the clinical impression of a minor kidney injury. Appetite was good, pain and tenderness had largely subsided and no further evidence of hematuria was noted on microscopic analysis; however, the patient continued to exhibit a low-grade fever. Retrograde urography was carried out on the fourth day of hospitalization. At this time, under general anesthesia, a large perirenal mass was palpated. This finding was corroborated by x-ray evidence of extravasated dye (fig. 2, *B*) outlining a mass surrounding the lower pole of the left kidney. Pseudomonas *aeruginosa* was cultured from material aspirated from the left ureter.

At operation, 5 days after admission, approximately 300 cc bloody urine surrounded the left kidney, which showed a complete transverse rupture (fig. 3) with wide separation of the upper and lower segments. The lower half, bearing the pelvis and attached ureter, was completely ischemic except for a narrow margin having an attachment through a small shred of capsule to the renal pedicle. The upper half, attached to a normally pulsating pedicle, showed only a marginal area of ischemia in its lower portion. Nephrectomy was carried out.

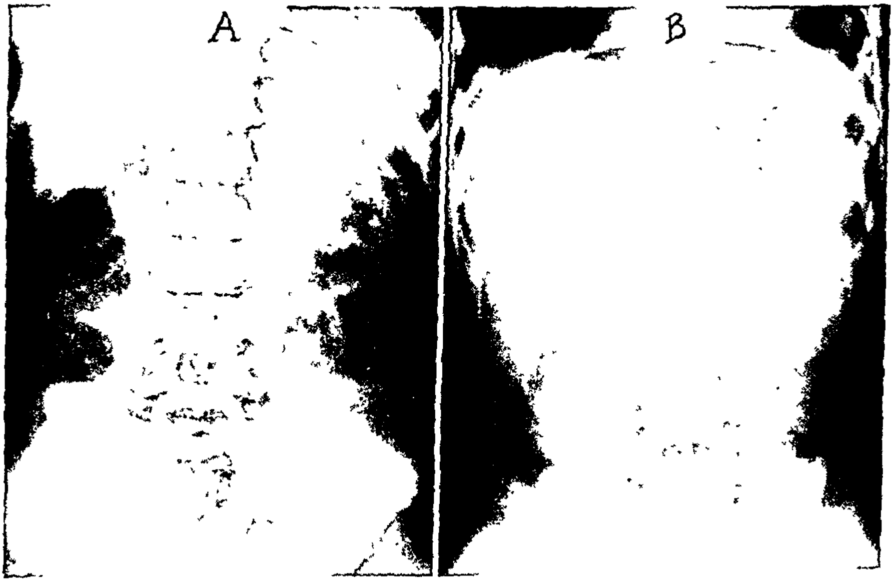

FIG. 2. *A*, excretory urogram. Prompt excretion of diodrast by injured left kidney. *B*, retrograde pyelogram; extensive extravasation of radio-opaque material surrounding lower pole of left kidney.

Convalescence was uneventful, and the patient was discharged on the sixteenth day of hospitalization.

Comment: The apparent integrity of this kidney, based on the prompt appearance and sharp delineation of dye excreted by the upper half of a completely transected kidney, resulted in a false sense of security and subjected the patient needlessly to the dangers of infection and secondary hemorrhage. Physical and laboratory examinations sustained the illusion of minor injury. Earlier retrograde investigation would have clearly indicated the need for surgical intervention and, while it is probable that the kidney would have been removed in any case, the period of hospitalization would have been materially shortened.

In contrast with the preceding case, the following instance may be briefly cited: R. H., a 13 year old colored boy, was admitted February 7, 1948, 4 hours after sustaining an injury to the left loin in a sledding accident. There was no evidence of shock. No mass could be palpated in the tender, splinted left loin. Hematuria was microscopic. Excretory urographic studies were inconclusive. Retrograde pyelography, 17 hours after admission, showed extravasation of dye from the left upper calyx. At operation, 40 hours after injury, 250 cc liquid and clotted blood were removed from the perirenal space. The upper $\frac{1}{6}$ of the kidney had been sheared off tranversely from the rest of that organ (fig. 4) and lay entirely free and without blood supply in the upper portion of the renal fossa. After removal of the separated fragment, the upper calyx was closed and the parenchymal defect repaired without nephrostomy drainage. Convalescence was complicated only by mild pyrexia; the patient was discharged on the 11th day of hospitalization. Follow-up 4 months later revealed good function without distortion in the repaired portion (approximately $\frac{5}{6}$ of the previously injured kidney).

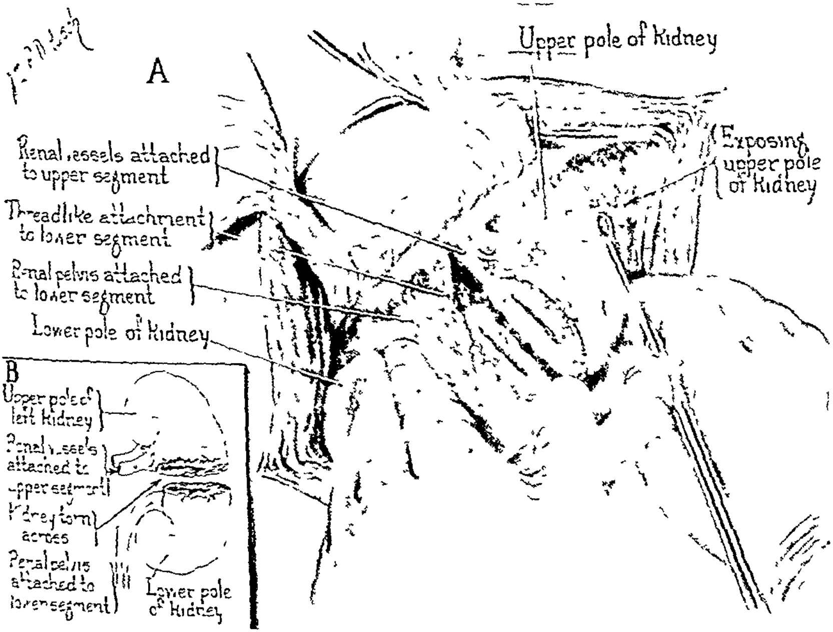
A
Upper pole of kidney
Renal vessels attached to upper segment
Exposing upper pole of kidney
Threadlike attachment to lower segment
Renal pelvis attached to lower segment
Lower pole of kidney
B
Upper pole of left kidney
Renal vessels attached to upper segment
Kidney torn across
Renal pelvis attached to lower segment
Lower pole of kidney

FIG. 3. Appearance at operation. Complete transverse rupture through midportion of left kidney.

Comment: Physical and laboratory examinations and excretory urography failed to accurately assess the major nature of the renal injury in this case. Early retrograde pyelography indicated the severity of the lesion and afforded a definite basis for proper therapy, i.e., operative intervention.

In all such cases in which the results of clinical investigation and excretory urography are indeterminate, we believe that prompt utilization of retrograde studies is imperative for intelligent management of the injury. Concern has been expressed in the past over the possibility of introducing infection and irritating foreign material into the perirenal tissues by this procedure. If aseptic cystoscopic technique is used, the risk of infection is minimal and is further reduced by the concomitant administration of antibiotic and chemotherapeutic agents. Since, moreover, the evidence of extravasation, in our opinion, constitutes a positive indication for surgical exploration, the presence of the foreign material will be only transient; the fear of complications arising from this procedure is far outweighed by the diagnostic value of the information that it affords.

Renal injuries of the type which have been defined as "major" do not, in themselves, constitute an immediate threat to life. The extravasation of blood and urine is limited by the tamponading confines of the perirenal fascia; an equilibrium is usually reached beyond which further extravasation occurs very slowly or not at all. It has been the feeling of many competent and experienced urologists, conditioned by their reluctance to hazard definition of the extent of the injury by retrograde pyelography, that such cases were best handled by expectancy until such time as the hand of the surgeon was forced by unfavorable developments. However, the accumulating evidence as to the high incidence and crippling effects of late complications, coupled with the increasing desire to conserve renal tissue whenever possible, has given weight to the belief,[7, 12, 19, 20, 21, 22, 23, 24] which the authors share, that early surgery is highly indicated.

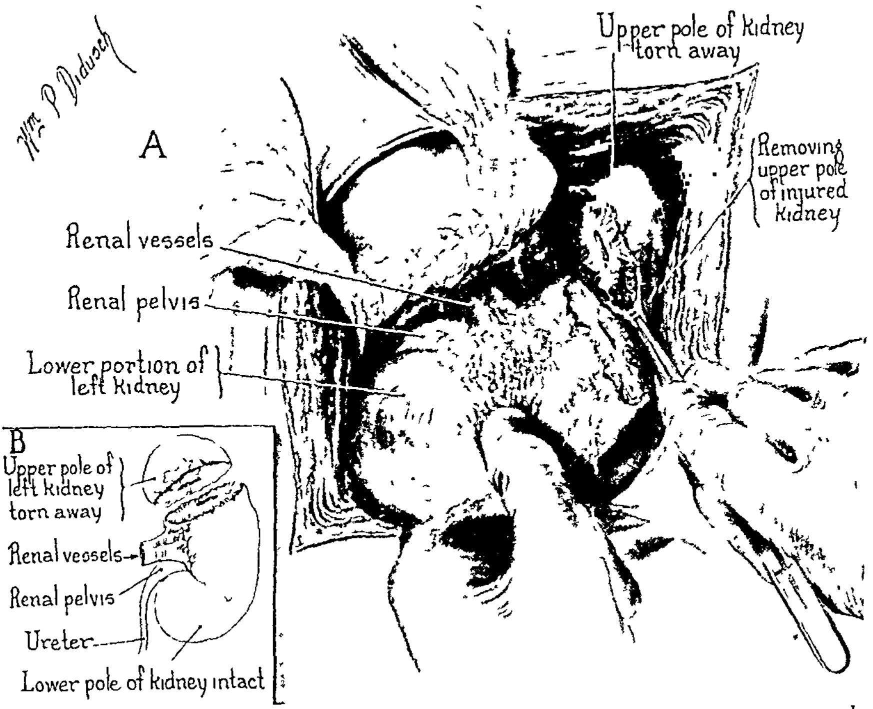
Wm P Didusch
A
Upper pole of kidney torn away
Removing upper pole of injured kidney
Renal vessels
Renal pelvis
Lower portion of left kidney
B
Upper pole of left kidney torn away
Renal vessels
Renal pelvis
Ureter
Lower pole of kidney intact

FIG. 4 Appearance at operation. Complete transverse rupture through upper pole of left kidney

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[19] Wood, A. H. J Urol., **37:** 437, 1937
[20] Farman, F.. J A M A , **114:** 210, 1940
[21] Lowsley, O. S and Menning, J H · J. Urol , **45:** 253, 1941.
[22] Campbell, M F · S Clin of N Amer , **21:** 443, 1941.
[23] Kindall, L E.· Calif & West Med , **49:** 115, 1938
[24] Kimbrough, J. C and Furst, J N J Urol , **59:** 807, 1948

After the initial shock, if present, has been overcome by supportive measures, a period of 48 to 72 hours usually ensues during which diagnostic and surgical procedures can be carried out without the mitigating influences of infection, secondary hemorrhage and general deterioration in the patient's condition. Proper surgical drainage, repair of parenchymal and collecting system lacerations, removal of devitalized tissue, and, if indicated, nephrectomy, are measures which, if carried out during this favorable period, find their justification in shortened convalescence and prevention of immediate and late complications.

Little controversy exists regarding either the nonsurgical management of minor injuries or the emergency operative treatment of critical injuries.

SUMMARY

A study of 71 cases of renal trauma is presented. There were no deaths. On the basis of the simplified classification described, the incidence in the various categories was: 1) minor injury, 47 cases (66.2 per cent); 2) major injury, 23 cases (32.4 per cent); 3) critical injury, 1 case (1.4 per cent).

Severe, unassociated renal disease was found in 6 cases (12.8 per cent) in the group of minor injuries, stressing the necessity for thorough urological investigation in every renal injury encountered. Frequently, the decision as to proper therapy to be employed, based on accurate definition of the degree of injury, was reached only after retrograde studies had been done.

The average periods of immediate hospitalization for major injuries treated surgically (19.1 days) and nonsurgically (20 days) were approximately the same.

No complications or sequelae attributable to the trauma were found in 7 out of 9 patients with major injuries who were treated by early surgical intervention. The remaining 2 cases could not be contacted for follow-up studies.

In contrast, of 14 cases with major injuries that were treated initially by nonsurgical means, 12 (84.7 per cent) exhibited renal disease of severe proportions on the previously injured side. It must be emphasized that the extremely high incidence of major sequelae in this series does not necessarily represent the true incidence in all cases of major injury treated nonsurgically, since 11 of the 14 cases were seen at this clinic only because of their sequelae. However, it does constitute a significant reminder that medical treatment may result in major sequelae in a not inconsiderable proportion of such cases.

CONCLUSIONS

Proper management of renal injuries is based on early and complete utilization of all diagnostic facilities necessary to accurately determine the extent of the injury.

Early operative intervention is indicated in all instances of major and critical injury.

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SPASM OF, AND ABSCESS FORMATION IN THE PSOAS MUSCLE CAUSED BY RENAL CALCULUS

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Inflammatory processes of the psoas muscle may be divided as follows:

A) Primary affections, cases in which the process is primarily located in the psoas muscle. Staphylococci, streptococci and pneumococci, present in the circulation, may cause psoitis.

As more clinical entities, we mention the acute idiopathic psoitis in children, the tropical myositis of the psoas muscle and the parasitic type caused by echinococci.

B) Secondary affections, cases in which the psoas muscle is involved secondary to neighboring processes.

As examples of this group are known: appendicitis, diverticulitis of the sigmoid, suppuration of a hygroma of the serous sac enveloping the psoas muscle spondylitis (mostly of tuberculous origin), intestinal perforations, pleuritis, osteomyelitis of the os ileum, foreign bodies, suppuration of nematomas (e.g. in hemophilia) and of iliac lymphglands. A few publications only are concerned with the uropoetic system causing a psoitis. Walters mentioned the association with double kidneys, Damm with perinephritis and Fernándex Bravo gave a description of a case with suppurative psoitis as a complication of calculous pyenephrosis. Behrman expressed the view that his 4 cases probably originated in the uropoetic system; also does McKenna.

As a typical example of such an origin we present the following case.

An emaciated woman of 64 was admitted to our hospital because during recent months, she became increasingly unable to stretch her left thigh. Previously she had suffered typical colicky attacks of pain in the left renal region Urinalysis at that time showed pus. These attacks had stopped a few weeks before her admission.

On general examination we found a painful spot in the lower left abdomen. The thigh was in adduction and 70 degrees flexion. The hip joint itself was normal and not painful. Examination of the blood revealed a chronic myeloid leukemia. The lymph glands, liver and spleen were not enlarged.

X-ray examination of the pelvis and hip joint was negative. As the cause of the contracted thigh was thought to be located somewhere in the psoas region an x-ray of the abdomen was made. A small round shadow was found at the level of L-4 and just proximal to the sacro-iliac joint. At first this shadow was believed to be a calculus inside the ureter. Excretory urography showed no function of the left kidney. This was confirmed at cystoscopic exploration. A catheter was easily introduced in the left ureter. A retrograde pyelogram showed clearly the shadow lying outside the ureter. The temperature was at times subfebrile.

The mild character of the chronic leukemia was no contraindication to the necessary operative exploration, because the impending complete invalidism.

Under ether anesthesia a typical curved lumbar incision was made. All that was left of the kidney was a small fibrous mass which, because of its perinephritic adhesions to neighboring formations, could not be removed without great risk. It was however possible to dissect the indurated wall of the renal pelvis and the arteries and veins to make sure that the whole mass was indeed the remainder of the left kidney. The ureter was easily freed and showed no signs of inflammation. Its appearance was entirely normal. Palpation of the psoas muscle revealed a swelling of 3 cm., approximately 12 cm. distal to the kidney. This was exactly the spot where on x-ray the shadow had been found. The edema and hyperemia gave the immediate impression of the presence of an inflammatory process inside the muscle. Incision showed pus (microscopically B. coli). By digital examination a calculus, the size of the stone of a cherry, was found inside the abscess cavity, and subsequently removed.

Its macroscopic appearance and chemical analysis (calcium oxalate) left no doubt as to its character of renal calculus. Moreover by probing the abscess cavity carefully, a tract inside the muscle was found leading in a proximal direction and finally communicating with the renal pelvis (fig. 1). The incision was enlarged and packed with gauze The wound was partially closed and traction applied to the left leg for a period of 4 weeks. After the removal of the gauze pack, the sinus track closed. Sulfadiazine and penicillin were administered for a period of 3 weeks. The spasm disappeared gradually and the patient made an uneventful recovery. The leukemia was unchanged at the time the patient left the hospital.

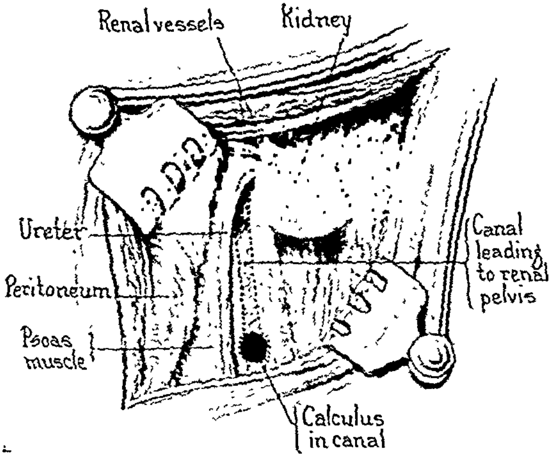

FIGURE 1

SUMMARY

In this case nephrolithiasis was complicated by perinephritis with subsequent perforation of a calculus through the wall of the renal pelvis into the psoas muscle. The clinical picture at the time of admittance in the hospital was the one that results from a spasm of the psoas muscle.

REFERENCES

BEHRMAN, S.: Lancet, 2: 297, 1930.
DAMM, E.: Ztschr. f. Urol., 26: 397, 1932.
FERNANDEZ BRAVO, E. A.: Rev. San. Mil. Habana, 8: 158, 1944.
MCKENNA, W. F.: Am. J. Surg., 8: 118, 1930.
WALTNERS, G. A. B.: Brit. Med. J., 2: 972, 1933.

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SPONTANEOUS DISINTEGRATION OF STAGHORN CALCULUS DUE TO RECUMBENCY

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The purposes of this study are to present a review of the accepted theories of renal lithiasis of recumbency and an unusual case of spontaneous disintegration of a staghorn calculus. In our search of the literature no case could be found on record that has shown the calculi to disintegrate and to be eliminated spontaneously. It is in the patient with multiple injuries, entailing complications and long periods of traction which prevent early ambulation, in which calculi develop. The cause of the formation of these calculi is not known or entirely understood. None of the many theories expounded fully explain the occurrence of these calculi. It is believed that early ambulation and the forcing of fluid have reduced the incidence of calculi of recumbency.

Demineralization of the bones following trauma and immobilization is apparently followed, in some instances, by an increased calcium output in the urine. However, protracted bed rest for other conditions such as heart diseases, tuberculosis, etc., is seldom followed by calculus formation. These formations appear to occur more frequently in those persons who have been vigorous and active and are suddenly rendered completely inactive due to immobilization following bone injury, particularly to the long bones. Stasis of the urinary tract, regardless of its nature, undoubtedly plays an important role in some instances. It is questionable whether hyperparathyroidism, hyperthyroidism, or hyperpituitary disease can account for the sudden formation of calculi following trauma and immobilization. It is also questionable if any metabolic disturbance, not already evident, such as gout, cystinuria, oxaluria, and xanthuria would suddenly become a factor due to a bone injury or immobilization.

Vitamin A deficiency in experimental animals has been proved to be a definite etiological factor in stone formation but conclusive evidence in man has yet to be demonstrated.

Infection of the urinary tract apparently plays an important role in the symptomatology presented by these patients, however it is increasingly evident that renal calculi of recumbency may occur in a sterile urinary tract. The infection that occurs is a secondary manifestation, resulting from trauma of mucosa and stasis of urinary flow, which present an ideal medium for bacterial invasion.

It becomes obvious that the causative factors productive of the calculi of recumbency are not known. Calcinuria is present in the majority of instances but not in every case. Here again the factors producing calcinuria are not understood. It has been repeatedly demonstrated that the inorganic constituents of the blood are within normal limits.

Read at annual meeting, Mid-Atlantic Section, American Urological Association, Hot Springs, Va., March 24, 1950.

It has been shown by numerous investigators that renal calculi following immobilization are composed of calcium phosphate in practically every instance. Calcium phosphate calculi, in contrast to other types of renal calculi, are rapidly growing, soft in consistency, and granular in architecture. It is recognized that these calculi are relatively symptomless. For this reason, these calculi may attain large dimensions and produce irreparable damage before their presence is recognized. Flocks[1] estimated that 5 to 15 per cent of all patients, immobilized for fracture with injuries to the extremities, develop renal calculi. However, in instances of paralytic vesical dysfunction, phosphatic vesical calculi occur in the majority of instances. Just what relationship exists between the occurrence of vesical calculi and renal calculi cannot be explained. This marked increase could be explained possibly on the basis of infection and stasis. Tully and Hawes[2] estimate the incidence of calculi in recumbency to be 0.6 per cent of all orthopedic patients treated.

It has been shown by various investigations that the time of appearance of renal calculi varies considerably. Tully and Hawes estimate the time of appearance to be 5 weeks to 33 weeks. This series of cases was in a temperate climate. Leadbetter and Engsten[3] estimate 8 days to 24 weeks. This series of cases was in a tropical climate and were possibly of a more acute nature. This wide variance of time of occurrence of symptoms cannot be explained but it is possible that climate may play a role. The incidence of bilateral or unilateral involvement varies in a similar manner. Tully and Hawes report bilateral involvement in 27 per cent of their cases, while Leadbetter and Engster report 57 per cent bilateral involvement. In contrast Priestley and Dunn,[4] in a survey of 382 patients with branched renal calculi not due to recumbency, report an incidence of 118 patients or 38.7 per cent bilateral involvement.

SYMPTOMATOLOGY

The usual symptoms presented by these patients are hematuria, either gross or microscopic, and pyuria, which may or may not become evident. The passage of small calculi spontaneously and the usual signs and symptoms which occur in ordinary calculus disease, such as pain at the costovertebral angle or radiating along the course of the ureter, or reflex pain to thigh and genitals, may be present. Many patients, however present no subjective symptoms. Diagnosis of their condition is made by both plain film and excretory urogram. These studies are always done in those patients who present abnormal urine findings or in whom subjective symptoms become evident.

CASE REPORT

W. R., a 24 year old white man, was admitted April 15, 1949, ten days following a motorcycle accident in which he sustained a severe cerebral concussion, compound fracture of middle left femur and simple fracture of right humerus with associated radial nerve injury. On admission the urinalysis showed no abnormal elements. Orthopedic immobilization was instituted. On June 6, 1949, urinalysis showed the appearance of a few red cells. On July 3, patient developed gross hematuria (fig. 1, *A*). Excretory urography, July 8, 1949, revealed a staghorn calculus on the left with multiple calculi in the left ureter and a partial staghorn on the right, with no marked evidence of obstruction to the dye bilaterally (fig. 1, *B*). The patient was ambulated with a brace on August 1, 1949 and 3 days later refractured the femur. He was again immobilized for a period of 3 weeks. Repeated urinalyses on August 2 through September 5 were negative.

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[1] Flocks, R. H.: J. Iowa M. Soc., 35: 331, 1945.
[2] Tully, G. C. and Hawes, L. E.: Surg. Clinic North Am., 26: 444, 1946.
[3] Leadbetter, W. F. and Engster, H. C.: J. Urol., 53: 269, 1945.
[4] Priestley, J. T. and Dunn, J. H.: J. Urol., 61: 194, 1949.

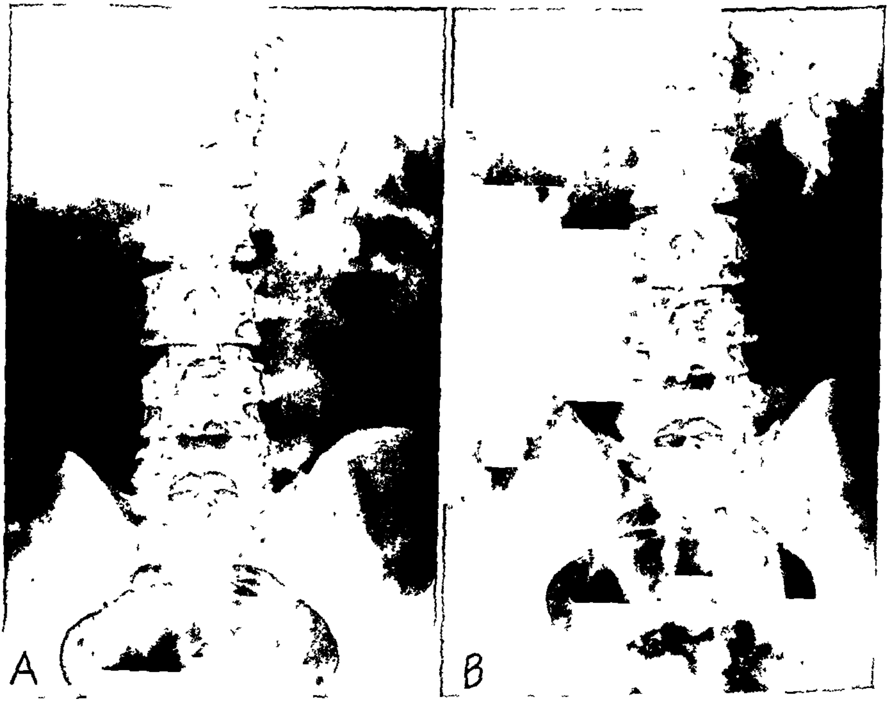

FIG. 1. *A*, showing bilateral renal calculi; on left, large staghorn formation. *B*, excretory urogram, 25 minute film, showing no impairment of renal function and minimal obstruction of left.

On September 1 the patient was out of bed. He was apparently well until September 10 when he noticed "sand" in his urine. On September 20, 1949, excretory urography revealed absence of calculi in the right and left renal areas (fig. 2). A large, smooth shadow of increased density was noted in the left lower ureter (4 by $1\frac{1}{2}$ cm.). The right kidney functioned normally. There was no function on the left. An attempt to catheterize the left ureter past the opaque shadow was unsuccessful. An extraperitoneal lower left ureterotomy was done. Myriad small calculi were removed from the lower portion of a markedly thickened and dilated ureter. The ureter was intubated and a roentgenogram immediately following surgery did not reveal any opaque shadow. The patient made an uneventful recovery. Urinalysis done 6 weeks following surgery was completely normal.

GENERAL MEASURES OF MANAGEMENT

A high fluid intake should be maintained. It is considered, in temperate climates, that an oral intake in excess of 3000 cc is adequate. The diet should be maintained in a well balanced ratio. The use of vitamins has been suggested but their efficacy has not been established. Eradication of urinary tract infection by the use of antibiotics or chemotherapy should be done. Manipulation and instrumentation of the urogenital tract is to be avoided unless specifically indicated. Any young individual, who requires immobilization for a prolonged period following trauma, should be subjected to complete roentgenographic study if he should present evidence of red blood cells, white blood cells or other symptoms of calculi.

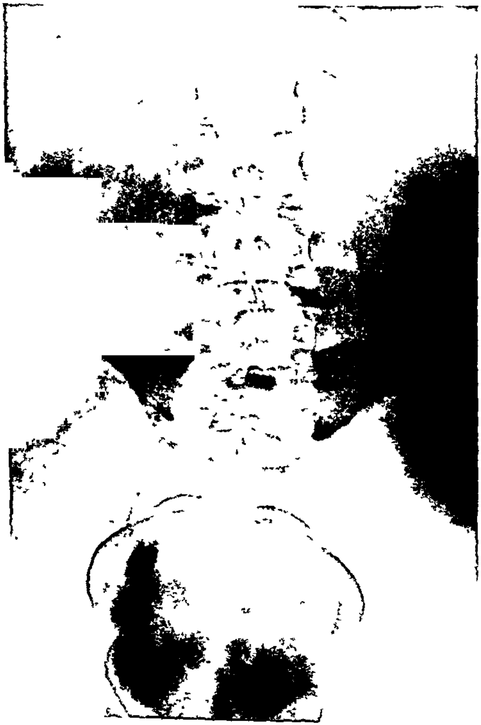

FIG 2 Showing complete absence of calculi in right and left renal areas. Large calcific density in lower left ureter.

Preliminary x-ray studies should be done periodically on all patients whose injuries necessitate a prolonged period of recumbency, in order to provide a basis for comparison and to rule out co-existent undiagnosed calculus disease.

Weekly urinalyses should be done.

Excretory urography should be done whenever objective or subjective signs or symptoms of calculus disease develop.

Late measures should calculi develop: Calculi may develop either with or without obstruction and infection.

Without the presence of obstruction and infection, the use of estrogens and aluminum hydroxide, as suggested by Shorr,[5] may be tried. The theory behind this treatment is that the estrogens increase the citric acid output which enhances calcium solubility. The aluminum hydroxide gels absorb phosphates from the intestinal tract. Shorr demonstrated that infection oxidizes citric acid thereby reducing the effect of the estrogens.

Cordonnier and Talbot[6] suggest the use of sodium acid phosphate as a means of reducing the excretion of urinary calcium. Cordonnier also has suggested intermittent irrigation of the renal pelvis by ureteral catheterization with solution G, an acidifying solution.

With obstruction, open operation is the only suggested therapy.

SUMMARY

Calcium phosphate renal lithiasis has been shown to occur frequently.

Calcium phosphate renal lithiasis produces few or no subjective symptoms even though extensive irreparable damage is not uncommon.

Early diagnosis is imperative and is usually made visually by urologic and roentgenographic examination.

Calcium phosphate stones may disintegrate and pass spontaneously as demonstrated by the case report. No previous report could be found of such disintegration.

Although various measures have been suggested for the treatment of renal calculi without obstruction, open surgery is the only procedure suggested for the treatment of calculi with obstruction.

1930 Chestnut St., Philadelphia 3, Pa.

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[5] Shorr, E.: J. Urol., 53: 507, 1945.

[6] Cordonnier, J. J. and Talbot, B. S.: J. Mo. Med. Assoc., 44: 179, 1947.

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ACUTE RENAL INSUFFICIENCY AND THE ROLE OF POTASSIUM WITH TREATMENT BY INTESTINAL LAVAGE

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The clinical condition known as "uremia" has long been considered to be a syndrome resulting mainly from the retention of waste products of nitrogen metabolism. Renal insufficiency by modern definition denotes the failure of the kidney to maintain the chemical equilibrium of various substances within the plasma and other fluid compartments of the body. It is more complex than the failure to excrete any single substance such as nitrogenous waste products which are normally removed from the body only by the functioning kidney.[1] Modern knowledge has demonstrated water and electrolyte inbalance as one of the most important factors in the production of this clinical state. It must be emphasized that water, nitrogen, sodium or other electrolytes may be affected singly or in multiple combinations depending upon the type of renal disorder. Failure due to intrinsic renal disease produces changes in the composition of the body fluids which are ultimately reflected in disturbed metabolism and function of the body cells. On the other hand, it should be stressed that functional renal disorders and insufficiency are in turn produced by extrarenal factors such as primary changes in the components of the tissue fluids, electrolyte loss or retention, and other profound chemical disturbances, in addition to heart failure, shock, and dehydration.[2]

The occurrence of hyperpotassemia with potassium intoxication in the type of acute renal insufficiency accompanied by anuria or severe oliguria was thought in the past to occur only on rare occasions.[3, 4, 5] A few cases of potassium intoxication associated with chronic renal insufficiency have been reported[6, 7] but in general the occurrence of potassium retention and subsequent intoxication with urinary suppression has never been appreciated as the serious medical emergency or problem that it represents. During the last war studies of deaths in patients developing acute anuria from renal tubular necrosis following muscle crush indicated that many sudden deaths were due to cardiac arrest as a result of hyperpotassemia.[8] Indeed, a recent report noted that 50 per cent of 26 patients with chronic renal insufficiency had some degree of hyperpotassemia.[9] It is likely

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Note by editor. The authors were awarded first prize for original research by the Committee on Scientific Exhibits for an exhibit on this subject at the annual meeting, American Urological Association, May 29–June 1, 1950.

[1] Harrison, T. R. and Mason, M. F.: Medicine, **16**: 1–44, 1937.

[2] Bell, E. T. and Knutson, R. C.: J.A.M.A., **134**: 441–446, 1947.

[3] Rabinowitch, I. M.: J. Biol. Chem., **62**: 245–258, 1924.

[4] Hoffman, W. S. and Jacobs, H. R.: J. Lab. & Clin. Med., **19**: 633–644, 1934.

[5] Myers, V. C., Croll, H. M. and Short, J. J.: J. Biol. Chem., **48**: 83, 1921.

[6] Marchand, J. F. and Finch, C. A.: Arch. Int. Med., **73**: 384–390, 1944.

[7] Keith, N. M. and Burchell, H. B.: Federation Proceedings, **6**: 343–344, 1947.

[8] Bywaters, E. G. L.: J.A.M.A., **124**: 1103–1109, 1944.

[9] Elkinton, J. R., Tarail, R. and Peters, J. P.: J. Clin. Invest., **28**: 378–388, 1949.

that electrolyte studies in the uremic patient in the future will reveal that potassium disturbances occur more frequently than believed in the past.

With modern knowledge of normal potassium metabolism various methods have been utilized in an attempt to control hyperpotassemia. It is well known that the kidney does not exert as much selective control over the maintenance of normal plasma potassium as it does over sodium which may be more selectively conserved or excreted in various pathologic renal conditions.[10] Potassium is the main cation within the cell and the largest portion is in combination with protein. Only approximately 25 per cent is in such an ionized state that it is available to pass back and forth across the cell membrane into the extracellular fluid.[11] Potassium concentration in the serum rarely varies to such an extent that serum osmotic pressures are disturbed as may occur with sodium. This is because potassium forms a relatively small percentage of the total circulating plasma cations (3.4 per cent). In conditions in which the renal secretion of potassium is blocked or greatly retarded as in acute anuria, the individual body cell tends to retain potassium so that hyperpotassemia does not readily occur in a majority of cases with renal insufficiency. When it is present a crisis of major importance is at hand.

In any treatment of acute renal insufficiency the potassium factor must be fully considered and it is obvious that a diet devoid of this electrolyte is first in order. Many foods, especially proteins and even fruit juices, contain potassium. The reduction of cell metabolism by diet and restricted muscular activity decreases protein catabolism and thus tends to augment the controlling intracellular potassium mechanism, a process which is reflected in a lowered serum potassium. Potassium anabolism within the cell also may be promoted by the administration of glucose and insulin which is protein saving.[11] The sparing of protein allows the cell protein to retain or bind more potassium with less tendency to hyperpotassemia such as readjustment of other electrolytes, especially sodium,[12] and the administration of calcium which is believed to counteract the toxic effects of potassium on the cellular physiology of myoneural junctions particularly those comprising the conduction system in the heart.[13] The basic difficulty with these procedures in an attempt to control elevated potassium blood levels is that they do not remove this electrolyte from the body once its high plasma concentration becomes a menace to cardiac function. The intestinal tract must be considered as a potential site favorable for potassium extraction.

It is known that under normal conditions four times the total plasma content of potassium is secreted into the gastro-intestinal tract each 24 hours, divided as follows:[14] stomach—approximately 23 mEq in 2500 cc volume; saliva—38 mEq in 1500 cc volume; bile—2.5 mEq in 500 cc volume; pancreatic secretion 3.2 mEq in 700 cc volume; and intestine—13.5 mEq in 3000 cc of secretion. There is thus an average total of 70 mEq in the 8200 cc of fluid secreted by various portions of the intestinal tract in a day.[15, 16] Almost all of this secreted potassium along with various other electrolytes and unknown substances are resorbed in the lower intestine. Interruption of this cycle of reabsorption seems a promising approach to the removal of potassium from the body in instances of hyperpotassemia with impending intoxication.

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[10] Peters, J. P.: Bull. N. Y. Academy Med., **25:** 749–763, 1949.

[11] Martin, H. E., Wertman, M., Westover, L., Simonsen, D. G. and Mehl, J. W.: Calif. Med., **72:** 133–141, 1950.

[12] Finch, C. A., Sawyer, C. G. and Flynn, J. M.: Am. J. Med., **1:** 337–352, 1946.

[13] Winkler, A. W., Hoff, H. E. and Smith, P. K.: Am. J. Physiol., **127:** 430–436, 1939.

[14] Fenn, W. O.: Physiol. Rev., **20:** 377–405, 1940.

The potential effectiveness of lavage of the intestinal tract in an effort to remove potassium was first considered and tried in a few patients in acute uremia by Hicks.[17] Several workers in the past have reported the successful use of lavage tubes of various types in different portions of the gastro-intestinal tract to remove only urea and possibly other nonprotein nitrogenous products in renal insufficiency.[17, 18, 19, 20, 21, 22] They demonstrated that it was possible in the majority of patients to irrigate the intestinal lumen with large volumes of fluid which were sufficient to remove appreciable urea. These results established the effectiveness of this method only as far as the use of large quantities of fluid and the extraction of urea were concerned, but the potassium and possible other electrolyte imbalances have been overlooked even in the reports on the use of the artificial kidney.

As a result of the promising report by Hicks in his first few cases of potassium intoxication, we undertook a systematic study of the effectiveness of lavage of the intestinal tract in the dog with the hope that it would be established as a relatively simple and efficient way to effect normal potassium balance in those instances of acute renal insufficiency complicated by hyperpotassemia. Two problems are involved in such an approach. The first is the development of an irrigating fluid which will remove a maximum amount of potassium and nitrogenous products with a minimum of distrubance to electrolyte, fluid and osmotic conditions within the circulating plasma and extracellular fluids. The second problem is evaluation of the relative efficiency of various sections of the gastro-intestinal tract which might serve as an excretory membrane to adjust any electrolyte imbalance, particularly that of potassium, in the absence of kidney function.

EXPERIMENTAL PROCEDURES

Dogs anesthetized with nembutal were employed in these experiments. The experiments were first carried out in normal dogs in which it was assumed that the intestinal secretions were normal. After establishing values in the normal, a series of experiments reported herein were designed as experiments in acutely uremic animals. Uremia was produced by bilateral ligation of the ureters or bilateral nephrectomy. The uremic dogs refused food, thus being deprived of exogenous potassium. The intracellular metabolic mechanisms under these cir-

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[15] Abbott, W. E.: Am. J. M. Sc., **211:** 232–239, 1946.

[16] Randall, H. T., Habif, D. V., Lockwood, J. S. and Werner, S. C.: Surgery, **26:** 341–363, 1949.

[17] Hicks, M. H., Crutchfield, A. J. and Wood, J. E.: Am. J. Med., **9:** 57–62, 1950.

[18] Vermooten, V. and Hare, D. M.: J. Urol., **59:** 907–919, 1948.

[19] Seligman, A. M., Frank, H. A. and Fine, J.: J. Clin. Invest., **25:** 211–219, 1946.

[20] Oppenheimer, G. D. and Rosenak, S. S.: J. Mt. Sinai Hosp., **14:** 908–911, 1948.

[21] Maluf, N. S. R.: J. Urol., **60:** 307–315, 1948.

[22] Brun, C.: Scand. J. Clin. & Lab. Invest., **1:** 344, 1949.

cumstances tend to regulate the plasma potassium concentration so that dogs in such states do not readily develop hyperpotassemia. In order that the potentiality of extracting potassium from plasma through the intestinal lumen might be explored in a state somewhat analogous to acute uremia in man, a condition of temporary hyperpotassemia was produced by the intravenous administration of potassium chloride preliminary to intestinal lavage. Potassium determinations on the plasma in these experiments as well as upon the perfusate solutions were carried out by means of the flame photometer using the internal lithium standard method.

The problem of devising a solution for intestinal lavage involves consideration of the electrolyte content of the normal plasma, and the electrolyte content of the secretion within the bowel. In the use of the artificial kidney a fluid has been used on the opposite side of a cellophane membrane from the blood which approximates plasma as far as osmotic pressure and the total cation and anion content are concerned. In reported experiments with the artificial kidney this fluid was devised simply to remove urea and possibly other nitrogenous products from the blood without disturbing the electrolyte equilibrium. Urea diffuses easily from the blood plasma into body cells, through cellophane and into the intestinal lumen. It apparently comes to equilibrium with the intestinal secretions or any fluids which are within the bowel lumen and presents no problem of extraction by any method.

It is necessary to use a solution which selectively extracts the desired substances to be eliminated and does not disturb or remove other electrolytes in the blood plasma. In the use of a cellophane dialyzer in the artificial kidney one is actually utilizing a filter which acts similar to Bowman's membrane in the glomerulus. In lavage of the intestinal tract one is dealing more with tissue which acts somewhat similar to the tubules of the nephron. It is not a simple semipermeable membrane through which various cations and anions diffuse but is lined by specialized cells which have selective function as regards absorption and secretion of various electrolytes and other substances. For an example, glucose does not diffuse readily across this membrane but must be phosphoralated before it enters the plasma from the bowel. The actual mechanism whereby electrolytes appear in the intestinal secretion is obscure.

The concentrations of various electrolytes vary in different levels of the bowel. For example, the secretions of the jejunum contain 111 mEq of sodium compared to 142 mEq of sodium in the plasma (table 1). The potassium and chloride of the jejunum are approximately equal to that of the plasma. Of the secretions of various portions of the intestinal tract, those of the jejunum simulate more closely the blood plasma than any other portion (table 2) and for this reason it would seem that the jejunum would be more ideal for effective lavage in an attempt to restore electrolyte balance.

Table 3 shows the composition of the solution used in these experiments. It can be noted (table 1) that the ionic equivalents of the perfusate solution is designed to be somewhat similar to the normal blood plasma and the content of the jejunum with the exception of the absence of potassium. In this way potassium should be extracted with the least disturbance of electrolyte equilibrium or fluid balance. The glucose content which is 2000 mg. per cent compared to the 100 mg. per cent in the blood makes the solution hypertonic so that any fluid exchange should be away from the plasma, a deficit which can promptly be replaced. Although we did not carry out freezing point determinations, the solution employed must closely approximate the osmotic pressure of the plasma and the jejunal secretion. Evidence of this is obtained from these experiments because the volume of recovered perfusate both in animals and in man was approximately the same as that injected. Neither the animal nor the patient gained or lost significant fluid, electrolytes, or body weight. The perfusate solution was made with tap water for use both in these experiments and in patients as there is no necessity for sterility.

TABLE 1. *Ionic equivalents*

	PLASMA	JEJUNUM	PERFUSATE SOL
Na	142 mEq	111 mEq	142 mEq
K	5 mEq	4 6 mEq	0
Cl	103 mEq	104 mEq	105 mEq
Ca	5 mEq		5 mEq
Glucose ..	100 mg. %		2000 mg. %

TABLE 2. *Acid base content of portions of G. I. tract (Peters)*

	TOTAL BASE	Cl	HCO_3
Fundus	40	160	
Pylorus	188	142	
Hepatic bile	182	90	45
Pancreas	168	115	45
Duodenum	177	120	
PLASMA	155	103	27
Jejunum	155	150	20
Ileum	162	80	90
Colon	162	80	92

TABLE 3. *Composition of perfusate solution*

NaCl	6 gm. per liter
$NaHCO_3$	3 gm. per liter
Ca Gluconate	.1 gm per liter
Glucose	20 gm. per liter

METHODS

1. Stomach. (a) Normal dog: A midline incision was made into the peritoneal cavity exposing the stomach. The pylorus was temporarily occluded by an en-circling rubber band and a Miller-Abbott tube then passed into the stomach. The interior of the stomach was lavaged with a Murphy drip using 3800 cc of the perfusate solution (table 3) over a 7 hour period.

(b) Dog in acute renal insufficiency and hyperpotassemia: Previous to lavage carried out as in the stomach of the normal dog, the ureters were ligated and divided and 4. mEq of potassium (as KCl) injected intravenously.

2. Duodenum. (a) Normal dog: The duodenum was exposed through an upper abdominal incision and a rubber band was placed around the terminal portion. A Miller-Abbott tube was passed through the esophagus and stomach well down into the duodenum. The duodenal lumen was lavaged with a Murphy drip using 3800 cc of perfusate solution over a 7 hour period.

(b) Dog in acute renal insufficiency and hyperpotassemia: Before perfusion of the duodenum, as in the normal dog, the ureters were ligated and divided and 4. mEq of potassium (as KCl) were injected intravenously in order to produce acute hyperpotassemia.

3. Jejunum. (a) Normal dog: In this experiment the jejunum was exposed through an abdominal incision and the duodeno-jejunal junction obstructed by a rubber band. A catheter was inserted into the proximal jejunum just distal to the rubber band by means of a Witzel jejunostomy. The jejunum was occluded 2½ feet from this afferent catheter while a second efferent catheter was inserted into the lumen through another jejunostomy at a point 2½ feet distal to the first. The lumen of the jejunum between these two catheters was lavaged with a Murphy drip using 3800 cc of the perfusate solution over a 7 hour period.

(b) Dog in acute renal insufficiency and hyperpotassemia: In these experiments the ureters were ligated and divided and the jejunum was perfused under the same experimental conditions as in the normal dog. Four mEq of potassium (as KCl) were next injected intravenously.

RESULTS

For purposes of simplification a single typical example of the results in each standard group is reported here as an illustration of the general results obtained. Additional individual experiments under identical conditions are not reported but revealed essentially the same results. In some further experiments uranium was employed to produce renal insufficiency and the amount of perfusate and duration of lavage were varied. These also yielded data consistent with the individual examples to be presented in detail. A total of 46 experiments were performed, irregularly divided among the standard and modified methods.

1. Stomach. (a) Normal dog: Results following lavage in a typical case of a stomach of a normal dog is shown in figure 1, *A*. It can be seen that the pre-perfusion total of plasma potassium in this dog was approximately 2.8 mEq. This figure of 2.8 total mEq was calculated on the assumption that 5 per cent of the total weight of the dog consisted of plasma, inasmuch as it did not seem necessary to us to carry out blood volume determinations for experiments of this type. After lavage of the stomach, it can be noted that only .156 mEq (7 mg.) of potassium were extracted. The post-extraction total plasma potassium content was essentially unchanged. The results in this case of a normal dog not

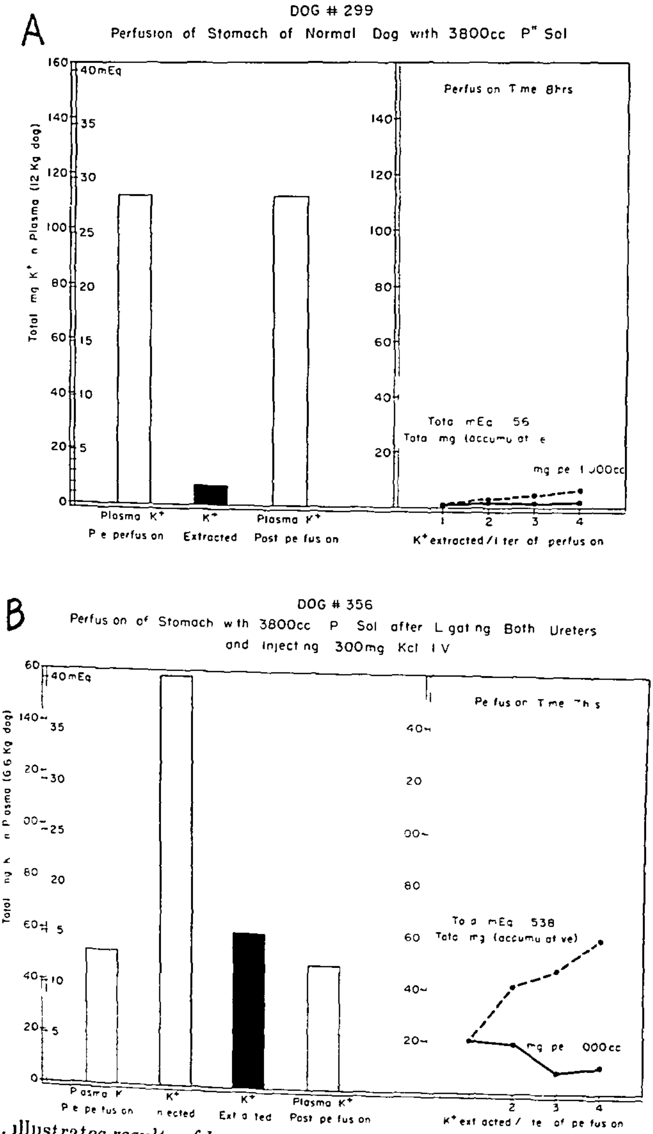

Fig 11, illustrates results of lavage of stomach of normal dog with 3800 cc of perfusate solution over approximately 7 hours During lavage process a total of only 0 156 mEq of potassium was extracted Plasma content was essentially unchanged In right section of 1, total accumulative amount removed is shown as well as amount extracted per liter of perfusate *B* illustrates results following lavage of stomach of uremic dog with hyper-potasemia Preliminary to lavage, 4 mEq of potassium (300 mg KCl) was injected intra-venously to produce hyperpotassemia As a result of a 7 hour lavage with 3800 cc of per-fusate, 1 54 mEq of potassium was extracted Post perfusion plasma content was slightly reduced from that prior to perfusion Total accumulative amount is shown in right section of figure as well as amount extracted per liter of perfusate

in renal insufficiency would indicate that the stomach is a relatively inefficient membrane for extraction of plasma potassium The amount of potassium in the perfusate per liter can be noted in the right section of this and the following

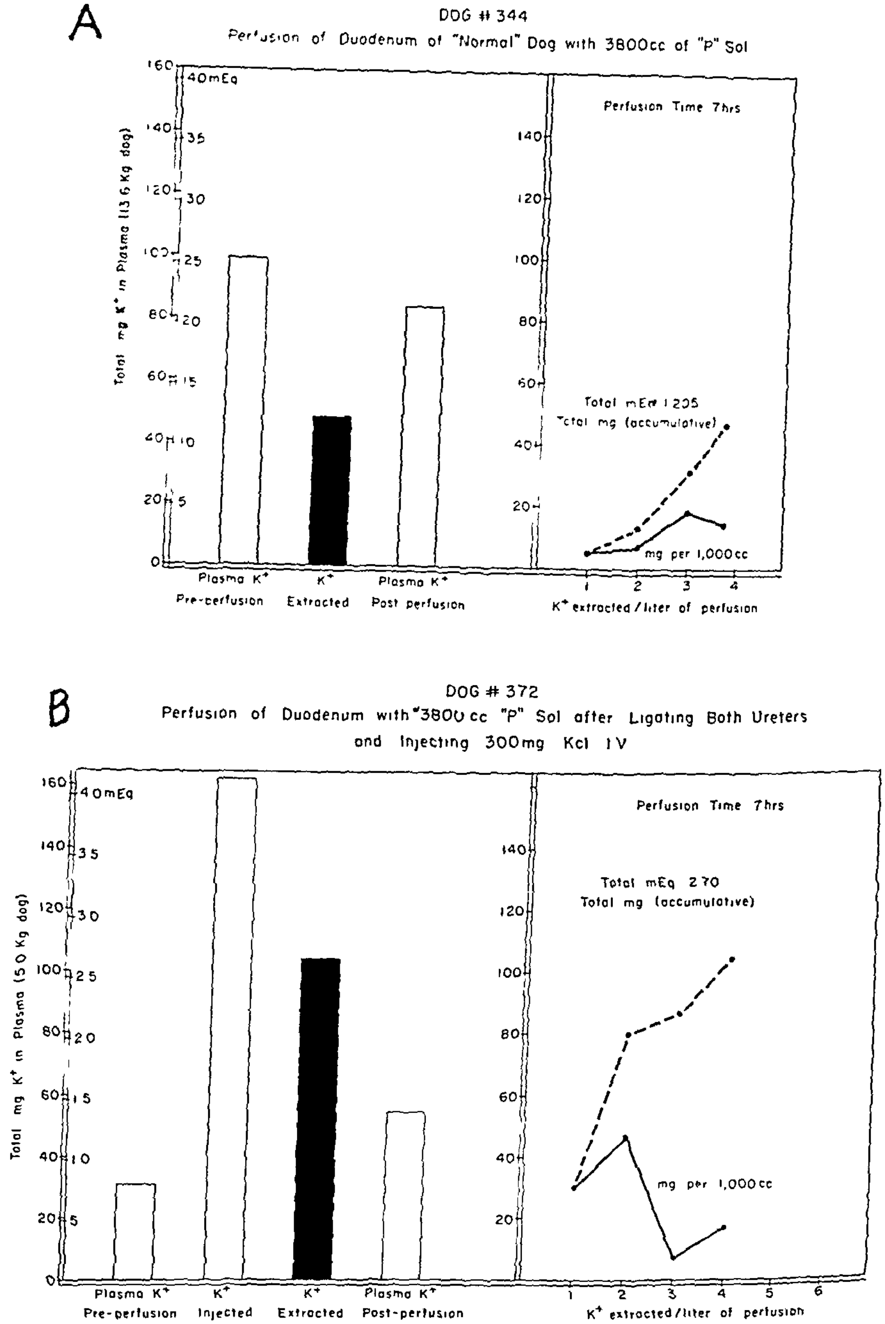

FIG. 2. *A*, illustrates results following lavage of a duodenum of a normal dog with 3800 cc of perfusate solution over a 7 hour period. A total of 1.20 mEq of potassium was extracted. Right section of *A* shows total accumulative amount and amount in mg. extracted per liter of perfusate. *B*, illustrates an experiment with lavage of duodenum with 3800 cc of perfusate over a 7 hour period immediately following ligation of both ureters. An intravenous injection of 4 mEq of potassium (300 mg. KCl) was given prior to lavage. During lavage 2.7 mEq of potassium was extracted.

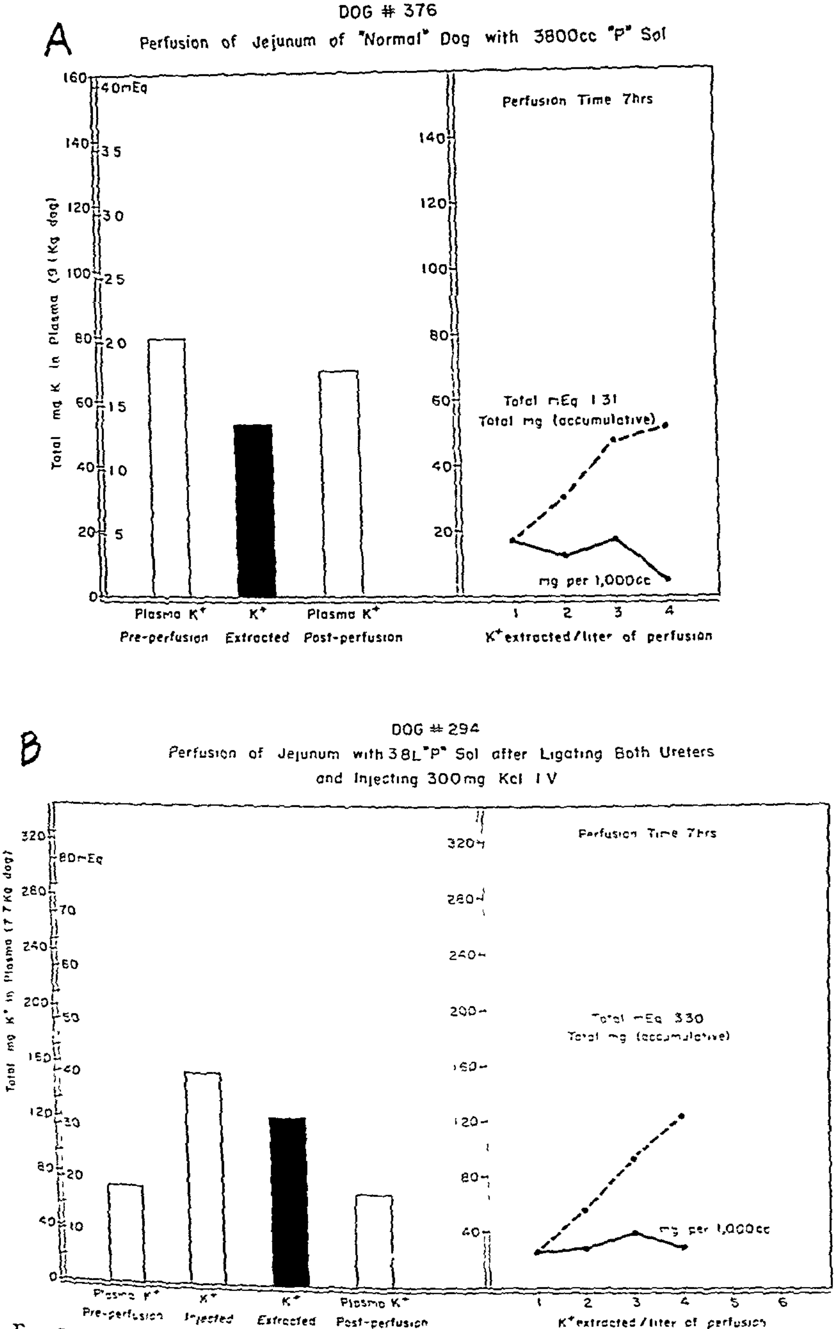

FIG. 3. *A*, illustrates results following lavage of jejunum of a normal dog with 3800 cc of perfusate solution over a 7 hour period. It can be noted that the preperfusion plasma content of potassium was approximately 2.04 mEq. During lavage process 1.31 mEq of potassium was extracted with reduction in plasma potassium content to 1.76. As noted in right section of *A*, a total of 1.31 mEq accumulated in perfusate was removed. *B*, illustrates results following lavage of jejunum over 7 hours with 3800 cc of perfusate immediately following ligation of both ureters and the injection of 4 mEq (300 mgm. KCl) of potassium. During lavage a total of 3.30 mEq of potassium was extracted. Right section of *B* shows accumulative amount extracted as well as amount per liter of perfusate.

figures as well as the total amount accumulating during the perfusion period. Further experiments exactly similar to this revealed essentially the same data as that shown in figure 1, *A*.

(b) Dog with acute renal insufficiency and hyperpotassemia: In the hyperpotassemic animal lavage of the stomach extracted 1.54 mEq of potassium (fig. 1, *B*). The pre-perfusion and pre-injection total plasma content was 1.3 mEq and following lavage it was 1.2 mEq. Compare this 1.54 mEq to the .156 mEq of potassium extracted from the stomach of the normal dog.

2. Duodenum. (a) Normal dog: After lavage, it can be noted in figure 2, *A* that approximately 1.20 mEq (47 mg.) of potassium was extracted. The pre-perfusion total potassium content of the plasma was approximately 2.5 mEq but after extraction it was reduced to 2.2 mEq. Reduction in plasma levels are not significant because of the cellular storage and release mechanism. Results in this experiment when perfusion is performed under similar experimental conditions indicate that the duodenum is more efficient than the stomach for removal of potassium.

(b) Dog with acute renal insufficiency and hyperpotassemia: The pre-perfusion total potassium content of the plasma was .8 mEq (fig. 2, *B*). (This dog only weighed 5 kg.) A total of 2.70 mEq of potassium was extracted in the perfusate. Compare the 2.70 mEq of potassium extracted in this experiment in which there was acute renal insufficiency and hyperpotassemia with only 1.20 mEq extracted from the duodenum of a normal dog above under similar experimental conditions. Such difference indicates the accentuation of potassium extraction by lavage when hyperpotassemia is present.

3. Jejunum. (a) Normal dog: Following lavage of a normal jejunum 1.31 mEq of potassium were removed (fig. 3, *A*). There was a reduction in total plasma potassium content from 2.04 to 1.76 mEq following this extraction.

(b) Dog with acute uremia and hyperpotassemia: It can be noted in figure 3, *B* that the pre-perfusion total plasma content was approximately 1.8 mEq. Following this determination 4 mEq of potassium (as KCl) was injected intravenously following ligation of the ureters. A total of 3.30 mEq of potassium was extracted. Compare this with only 1.31 mEq extracted from the normal jejunum as depicted in figure 3, *A*.

DISCUSSION

It is evident from the data in these experiments that the electrolyte potassium is easily extracted from the intestinal lumen of the dog by lavage. In the data mentioned previously, we stated that the normal human stomach secreted 22.5 mEq of potassium in 24 hours compared to only 13.5 mEq for the small intestine. Added to this 22.5 mEq in the stomach is 2.5 mEq in the bile and 3.22 mEq in the pancreatic secretion in 24 hours, making a total above the ligament of Treitz, except for that secreted in the saliva, of 28.22 mEq as compared to the 13.5 mEq secreted in 24 hours for the remainder of the intestinal tract. From this, one would expect the stomach and duodenum to be far more efficient than any other section of the intestinal tract. In our results in the dog and unpublished data of lavage in man we found the stomach and duodenum relatively inefficient. When the mucous membrane of the stomach and duodenum come in contact with the perfusate solution the cells of these organs do not act as a dialyzing or secreting membrane for potassium as readily as do those of the jejunum. One might conclude that the cells of the jejunum have more inherent capacity to secrete potassium into a slightly hypertonic and essentially isosmotic perfusate or else that they act as a better dialyzing membrane. This certainly seems to be the case as regards the jejunum in the dog, and our experiments in man confirm this finding. The efficiency of the stomach, duodenum and jejunum increases greatly in that order.

The data here also clearly indicate that potassium comes across the membrane of stomach, duodenum and jejunum more readily when there is an excess in the plasma and extracellular fluids. A comparison of lavage of the normal jejunum with that of the jejunum in an animal with hyperpotassemia (fig. 3) shows that it was possible to extract about three times the amount of potassium when total renal insufficiency and hyperpotassemia were present. The latter state somewhat simulates that which occurs in patients with acute anuria or severe oliguira and especially in those patients in whom the potassium intake has not been deleted in the diet following the renal injury.

The above experiments involving the stomach, duodenum and jejunum clearly indicate the ease and feasibility of extracting potassium from the jejunal portion of the gastro-intestinal tract in the dog, but it should be emphasized that the results of experiments in animals cannot always be completely translated into the physiology of man. However, the data obtained here tend to substantiate the feasibility of controlling hyperpotassemia and intoxication by intestinal lavage.

REMOVAL OF UREA BY LAVAGE

There has been no difficulty in the past in extracting urea from the plasma by lavage of the stomach, pleura, or peritoneum, or by the artificial kidney. Lavage of the intestinal tract in both animals and man has confirmed the ease of extracting urea.[17] [18] [19] [20] [21] Urea is nonelectrolytic and diffuses across membranes and into body cells with ease. Approximately $\frac{1}{3}$ to $\frac{1}{2}$ of the urea in the glomerular filtrate diffuses back across the cells of the tubules into the blood plasma so that it is not cleared completely even by the kidney. It can be noted that the perfusate solution (table 3) used in these experiments contained no urea. Urea will accumulate in solutions present in the intestinal tract where an equilibrium is soon established with the plasma concentration. There is no evidence that it contributes in any way to the condition known as uremia. It has been well established that urea is a nontoxic substance; Gamble has stated that it is fortuitous in chronic nephritics that the blood urea is elevated because, in such patients who have a reduction in glomerular filtration, the elevated blood concentration allows this substance to pass more readily into the filtrate and out the kidney with more efficiency and less cellular work. Intravenous injection of urea in man is harmless.

During the potassium extraction procedures outlined in these experiments, the perfusate was analyzed for the content of urea in all instances. Figure 4 depicts the extraction of urea in nine of the experiments. These results shown in figure 4 were all in experiments in which the jejunum was used during the extraction of potassium. They were all approximately over a seven hour period in which varying amounts of the perfusate solution were used. The maximum amount of urea extracted during any perfusion was 6.4 gm. urea. This is at the rate of 22.14 gm. in 24 hours. Extracting urea by lavage of either intestinal tract or peritoneum is relatively simple and a fall in plasma urea as much as 100 mg. per cent can be accomplished in a short period. In one perfusion experiment of the jejunum in a dog with acute renal insufficiency the pre-perfusion plasma level was 606 mg. per cent. After slightly over 7 hours of lavage in which 5 liters of solution was used the blood urea was reduced to 389 mg. per cent.

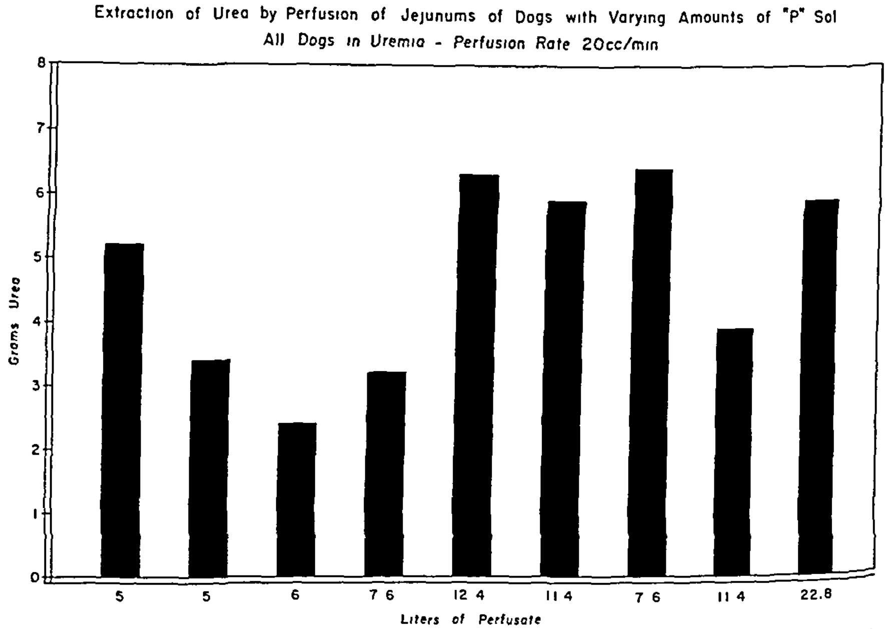

FIG. 4. Illustrates removal of urea during some of previous experiments in which potassium was being extracted. Results in this figure are in 9 instances in which jejunum was lavaged with varying amounts of perfusate solution. All dogs in these experiments were in acute uremia either as a result of bilateral ligation of ureters, bilateral nephrectomy, or following intravenous injection of uranium acetate. Rate of perfusion was approximately 20 cc per minute. It can be noted in 4 experiments that approximately 6 gm. of urea or more was removed during a standard lavage procedure.

Hicks[17] extracted 49.5 gm. urea from one patient in 24 hours with lavage of the jejunum using 24 liters of perfusate. Most individuals excrete approximately 15–25 gm. of urea in a day. We believe it is unproved that any patient has been benefited, or any lives saved, by removing urea whether by artificial kidney, intestinal lavage, peritoneal dialysis, or cross-transfusions. It is more likely that fatalities in uremia with reversible renal injuries have been due to electrolyte and water imbalances, cardiac failure from hydremia, and retention of unknown and known toxic substances such as phenols, guanidine, paracresols, and indican.

CLINICAL IMPLICATIONS

From the preliminary observation by Hicks[17] in a few patients with dangerously elevated serum potassium levels, extraction by intestinal lavage and reduction of the hyperpotassemia were carried out with as little difficulty as in our animal experiments. It is admitted as far as man is concerned that an occasional patient might be encountered in whom nausea would be so severe as to prevent passage of a Miller-Abbott tube far enough down into the jejunum, where according to these experiments most effective and efficient extraction would be possible. A jejunostomy approximately five to six feet below Treitz's ligament has alternatively been suggested. In this case it would be necessary only to pass a Levine tube to the stomach with the lavage fluid finding egress through the jejunostomy. We have not as yet resorted to this procedure but it might be necessary if it were impossible to pass a Miller-Abbott tube. If a patient is encountered with anuria, it would be propitious to start the tube down soon after admission in anticipation of lavage in case urinary secretion was not spontaneously resumed. Studies on the more readily available large intestine are in progress and will be reported later.

Clinical Example of Control of Dangerously Elevated Potassium in Patient with Acute Renal Insufficiency

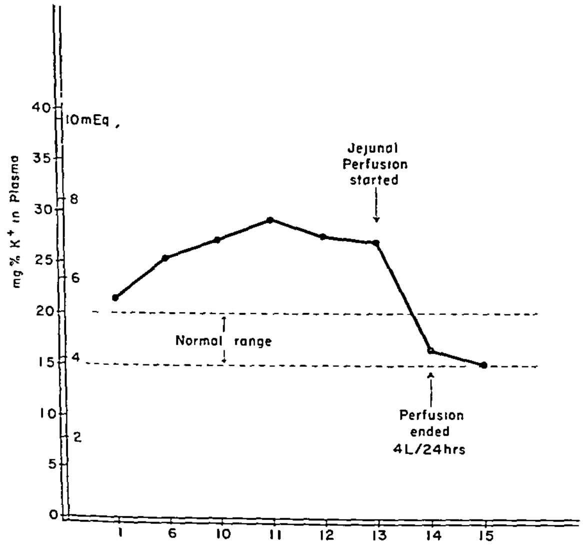

FIG. 5. Illustrates clinical example of lavage for control of a dangerously elevated serum potassium in a patient with acute renal insufficiency. Patient was admitted with prostatic obstruction and moderate oliguria and an elevated blood urea. During ensuing days following admission plasma potassium gradually rose to above 7 mEq per liter. Seven mEq per liter is a critical level above which cardiac toxicity occurs. Perfusion of jejunum was started on twelfth day and 4 liters of perfusate used over a 24 hour period. It can be noted that plasma level of potassium quickly returned to within normal range.

Clinical experiences with this method of control of hyperpotassemia are also to be reported later, but figure 5 illustrates the ease of extraction of potassium clinically by lavage of the jejunum. This patient, WS, UVa. Hosp. No. 292950, was a man admitted in March 1950, with prostatic obstruction and a blood urea of 122. The plasma potassium was 5.5 mEq. After admission to the hospital the blood urea gradually rose to 200 mg. per cent on the ninth day with some

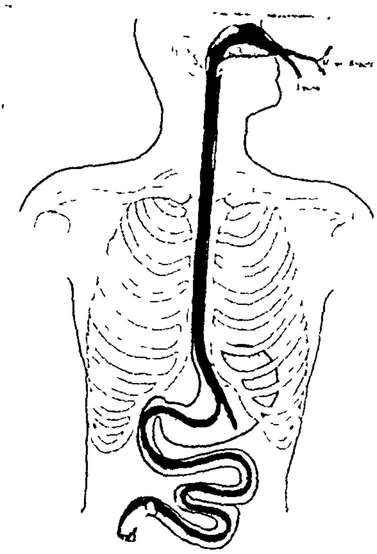

FIG. 6. Illustrates position of Miller-Abbott and Levine tubes for jejunal lavage. Miller-Abbott tube is passed first to a position approximately 5 feet beyond pylorus. This is usually confirmed with fluoroscopy. Levine tube then inserted through other nostril down into stomach. Perfusate solution enters Levine tube at a rapid rate by means of a Murphy drip. It is aspirated from distal end of Miller-Abbott tube in jejunum with suction by a Wangensteen apparatus.

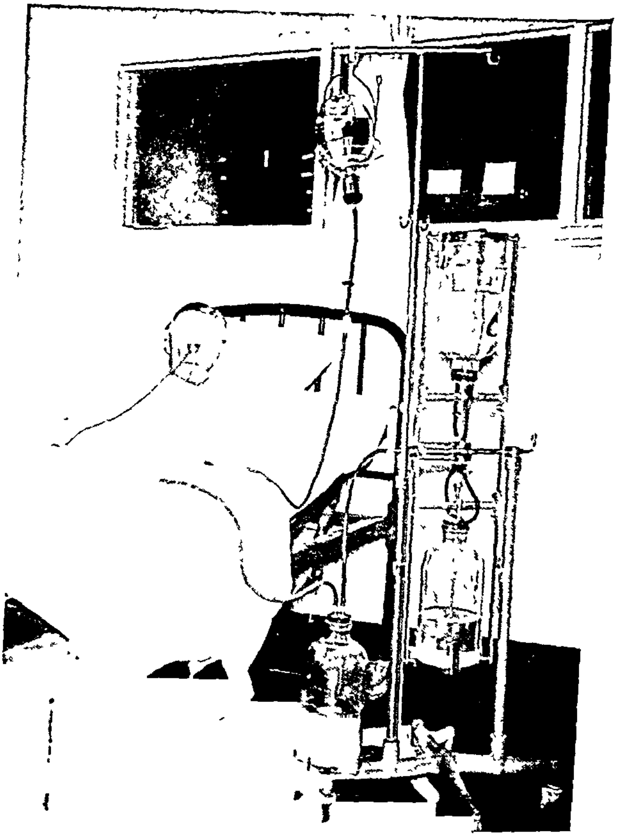

FIG. 7. Illustrates patient referred to in figure 5. It shows Levine and Miller-Abbott tubes in place. A Murphy drip carries perfusate through Levine tube and aspiration from jejunum is by means of an ordinary Wangensteen apparatus.

degree of suppression of urinary secretion and a gradual rise in serum potassium. It can be noted that on the eleventh hospital day, the serum potassium had reached 7.5 mEq. Concentrations above this critical level result in severe electrocardiographic changes with the potentiality of cardiac standstill and death. On the fourteenth hospital day a Miller-Abbott tube was passed well down into the jejunum and a Levine tube into the stomach (fig. 6). The correctness of the position of the Miller-Abbott tube was ascertained by fluoroscopy. Irrigation of the upper gastro-intestinal tract and especially the jejunum was carried out with the described perfusate. The solution was allowed to run at a constant rate through the Levine tube into the stomach and aspirated through the Miller-Abbott tube by means of a Wangensteen suction apparatus from the jejunum

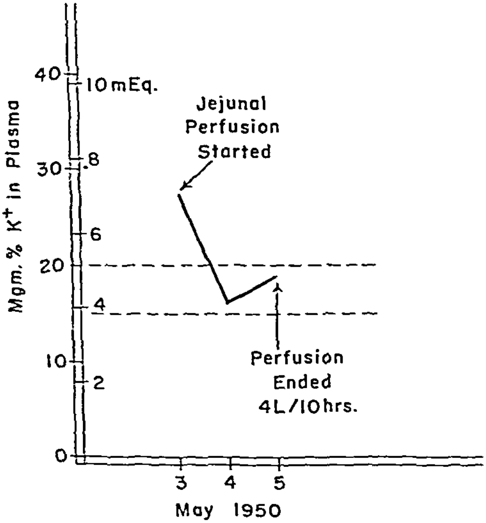

FIG. 8. Illustrates potassium plasma level in a patient with hyperpotassemia as a result of renal disorder in which sodium was not being conserved by kidney. For some reason potassium was retained and hyperpotassemia resulted. When plasma potassium had reached critical level of 7 mEq, jejunal perfusion was started and within 10 hours using 4 liters of perfusate there was a preciptious reduction in potassium plasma level to within normal range.

(fig. 7). In a 24 hour period, approximately 4 liters of perfusate was employed. It can be noted in figure 5 that the serum potassium was precipitously lowered to within the normal range. Further perfusion in this patient was not necessary because of the rapid return to normal plasma levels. During lavage of the jejunum, it was found that the return of the 4 liters of perfusate contained 4.46 gm. of urea, 0.6 gms. of uric acid, 1.48 gm. of creatine, and 0.63 gm. of potassium (16.1 mEq). A normal man of this patient's weight has in his plasma a total of approximately 0.7 gm. of potassium (17 mEq) and during this period with lavage of only 4 liters of perfusate, an amount equivalent to approximately his total plasma potassium content was removed. It is possible to perfuse with large amounts of fluid when necessary and in one case Hicks[17] perfused the jejunum with 24 liters over a 24 hour period.

Figure 8 shows another instance in a patient with hyperpotassemia in whom the jejunum was lavaged with 4 liters of perfusate in 10 hours. This treatment precipitiously reduced the elevated serum potassium to within normal limits. It is necessary in clinical cases to follow the plasma potassium every 2 hours, because in one of our patients, potassium was removed to such an extent that the blood concentration was reduced to 2.5 mEq and characteristic changes of hypopotassemia appeared in the electrocardiogram.

It was seen from results in animals and those we have encountered in man so far that lavage of the upper intestine is just as efficacious as the artificial kidney or any other method for removal of electrolytes or urea. When compared to the artificial kidney, it is not so rapid but far less complex and essentially without hazards. Further clinical studies in our opinion will confirm the efficacy of removing potassium and adjusting electrolyte balance in severe reversible renal insufficiency by intestinal lavage.

SUMMARY

Therapy in acute uremia with anuria or severe oliguria must include a consideration of electrolyte imbalance and especially potassium concentrations in the body fluids. Electrolyte imbalance may play a more significant role in acute uremia than has been thought in the past. Indeed, the retention of urea and possibly other nitrogenous products is easily reduced with intestinal lavage, but emphasis is placed on the control of potentially dangerous elevations of serum potassium in acute uremic states. Potassium levels above 7.5 mEq may lead to potassium intoxication and sometimes the characteristic sudden death that occurs in acute uremia. The signs and symptoms of hyperpotassemia are bradycardia, dyspnea, respiratory paralysis, coma and cardiac standstill preceded by characteristic electrocardiographic changes. Sudden death is a feature of such intoxication.

This study demonstrates the ease of removing potassium from the blood plasma by lavage of the upper small intestine of the dog and in clinical cases. Intestinal lavage for removal of electrolytes and urea is far more simple than the use of dialyzing membranes (artificial kidney), and other reported methods such as peritoneal lavage and cross transfusion.

These experiments were made possible by the cooperation of Mr. Boyd Perry, Miss Kay Irvine and Miss Ione K. Shield in the Department of Surgery Research Laboratory.

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PERIRENAL CYST ASSOCIATED WITH HYPERTENSION: REPORT OF A CASE

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Perirenal cyst is a rare clinical entity. A review of the literature revealed only 2 reported cases. Perirenal cyst must be distinguished from pararenal cyst because of statistical as well as etiological implications. Gutierrez in 1942 classified large solitary cysts of the kidney and made a definite demarcation between the two types. The perirenal cysts are intimately associated with the fibrous renal capsule, as opposed to pararenal cysts, which are not only external to the renal cortex, but also the fibrous renal capsule. Neither is directly associated with renal substance.

ETIOLOGY

From the etiological standpoint, it is difficult to explain a cyst so intimately associated with the renal capsule on a developmental basis. Histologically, the capsule is composed mostly of fibrous connective tissue and scattered elastic connective tissue, with no cellular elements capable of cyst formation. The possibility of embryonic rests from the wolffian or müllerian ducts, however, is a possibility not to be ignored. Trauma with hematoma of the renal capsule and subsequent cyst formation from an organized hematoma is a definite possibility. The etiology in one of the previously reported cases was not established because of lack of specific structure. In the other, trauma as the etiological factor was implied from the history, and probably justifiably so; but microscopically the cyst was nonspecific in character. In the case reported here there were no previous signs or symptoms suggestive of renal trauma or any other genito-urinary tract disease, and the etiology is definitely obscure.

CLINICAL PICTURE

Shih and Wu reported a case of a Chinese housewife, 38 years of age, who began having a dull aching pain in the right flank 3 months before admission. The pain was exaggerated on deep respiration and gradually subsided in 6 weeks. With disappearance of the pain she began to notice a firm, round mass in the right upper quadrant, which grew slowly, but was nontender. Urinary symptoms were absent, but there had been some weight loss and loss of strength. There was no history of trauma. Physical examination revealed a firm, smooth, round and nontender mass which extended 10 cm. below the costal margin, palpable in the right upper quadrant. Otherwise, physical examination was normal. Retrograde pyelogram revealed marked displacement of the right renal pelvis, calyces and ureter, with marked narrowing and compression of the middle calyx. A preoperative diagnosis of malignant neoplasm of the right kidney was made and preoperative irradiation given. A transperitoneal nephrectomy was done.

The other reported case, by Baudin and Delclaux, was of a 30 year old French laborer who had sustained a rather severe blow to the right lumbar region 15 years previously. He had gross hematuria for 4 to 5 days, and conservative management with bed rest was the *only treatment instituted*. Right upper quadrant and right flank pain was present intermittently during the 15 year interim A pyelographic diagnosis of probable tumor of right kidney was made, and a nephrectomy done.

The case reported here was completely asymptomatic from the genito-urinary tract standpoint. He had a hypertension of 160/110, preoperatively. A pyelographic diagnosis of left renal cyst or neoplasm was made, and a transperitoneal nephrectomy done.

PATHOLOGICAL DATA

In the reported case first mentioned the gross specimen was described as a "cystic mass 13 by 10 by 7 cm. on one side of which is attached a much compressed kidney. The cyst wall is composed of dense fibrous tissue measuring from 1 to 3 mm. in thickness. The cavity contains fibrin and about 150 cc. of dark-colored fluid. On the medial side the cyst wall comes into contact with the lateral aspect of the kidney and is fused with the renal capsule. The kidney and renal pelvis are markedly compressed. Microscopically, the cyst wall consists of dense fibrous tissue. In the inner part of the wall are numerous strands of fibrin, and where not covered with fibrin, it is lined by a layer of flat elongated cells. Section through the portion in contact with the kidney shows that the cyst wall and renal capsule are fused. The renal cortex shows moderate atrophy at the periphery."

In the second reported case the description was similar except for moderate calcification of the cyst wall. The cyst was continuous with the renal capsule and stripped with it from the renal cortex with ease.

The case reported here is quite similar in that there was fusion of the cyst wall with the capsule without any involvement of the kidney substance except in pressure atrophy. There was mottled calcification in the wall of the cyst.

CASE REPORT

H. W., Register Number 29829, a 22 year old white man, was admitted to the Veterans' Administration Hospital at Louisville, Kentucky, June 8, 1949 complaining of intermittent pain, swelling, giving away and locking of the left knee. The first episode occurred during football practice in September 1948. Surgical treatment was recommended, and he was admitted for that purpose. A review of systems revealed that the patient had had intermittent mild to moderate occipital headaches for the past 5 to 6 months. No other symptoms were manifest. Past history and family history were not remarkable.

Examination revealed a young man of athletic build not appearing acutely or chronically ill. The blood pressure was 160 108. The left knee was slightly swollen with some demonstrable effusion. There was no limitation to motion, and there was only slight pain on extremes of motion. The heart presented no abnormalities and fundiscopic examination was normal.

Complete blood count and complete urinalysis were negative. Kahn (blood), negative. Numerous repeat urinalyses were negative. Chest x-ray, negative. X-ray left knee, negative. Nonprotein nitrogen 33 mg. per cent. Excretory urogram (July 1, 1949) revealed that the right kidney shadow was normal in size, shape and position and showed prompt excretion of the contrast medium. The calyces, pelvis and ureter were normal. The left kidney outline was indefinite. The psoas shadow was sharp, however. There was prompt excretion of contrast medium, but there was considerable distortion of the calyceal pattern with medial displacement of the lower calyx and renal pelvis, and superior and medial displacement of the middle calyx. A left retrograde pyelogram (July 11, 1949) revealed findings similar to those of the excretary urogram on the anteroposterior view (fig. 1). The left lateral view revealed moderate anterior displacement of the left kidney and ureter. The perirenal air insufflation did not outline the kidney completely, and this study was inconclusive. Electrocardiogram (June 17, 1949) was normal.

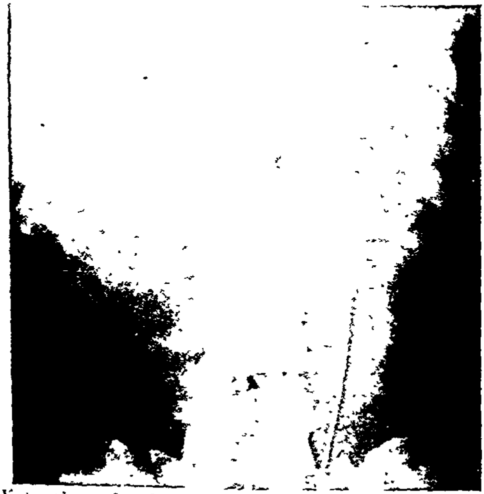

FIG. 1. Showing distortion of pelvis and calyces, left kidney. Excretory urogram done previously revealed normal outline on right.

A diagnosis of ruptured medial meniscus of the left knee was made, and the patient was taken to the operating room June 16, 1949 for surgery on the knee. The patient was given a spinal pontocaine anesthetic with 3 mg. neosynephrin. Ephedrine sulfate 25 mg. was given subcutaneously, just prior to the spinal anesthesia. Ten minutes later he developed a sudden, severe, generalized headache and his blood pressure read 260 120. The pulse was regular in rhythm, and the rate was 76. With intravenous pentothal sodium, and after 40 minutes, the blood pressure was still 200 100, and surgery was canceled without the incision being made. One hour after the spinal, the blood pressure was 170 100 and in 1½ hours had returned to 150 90. The patient was transferred to the medical service for workup of hypertension. An excretory urogram was done, in accordance with the routine medical workup for hypertensive cases in this hospital. A histamine test was done for possibility of pheochromocytoma and revealed elevation of blood pressure from 162/88 to 212/94, with a return to normal in 4 minutes. The blood pressure varied, while under medical observation, from 150/86 to 160/110.

When the information of a mass lesion of the left kidney became known, the patient was transferred to the urological service. The blood pressure (July 21, 1949) was 160/110. On July 22, 1949, under pentothal, gas-oxygen-ether anesthesia, the left kidney was explored through a left upper quadrant transverse transperitoneal incision. Palpation of the kidney revealed a mass in the middle third which was quite hard, nodular and resistant to pressure. It was believed that the lesion in question was a malignant tumor, and without further manipulation of the kidney, the pedicle was isolated, clamped and ligated. An extracapsular, extrafascial removal of the kidney was done. Gerota's fascia was separated from the surrounding tissues with difficulty because of rather dense adhesions. The regional lymph nodes were normal. The patient tolerated the procedure well. The postoperative course was entirely uneventful. The blood pressure on the first postoperative day was 126/78 and on the eighth postoperative day was 118/78. He was discharged on the tenth postoperative day.

Pathological report: "The gross specimen is a kidney weighing 196 gm. and measuring 12 by 7 by 4.5 cm. The medial portion contains a cyst measuring 6 by 3.8 by 5 cm. The cyst has a dense hyaline, gray-white wall in which small, gritty deposits of calcium salts can be felt. The thickest portion of the capsule, 0.8 cm. wide, is at the medial and posterior surfaces of the kidney. Here the outer wall of the cyst feels nodular. The nodules contain deposits of calcium salts and appear partially necrotic and caseous. The lateral portion of the cyst compresses the kidney substance so that the compressed cortex and medulla are only 2 cm. thick. The renal pyramids are poorly defined, and the cortex and medulla indistinctly demarcated. The renal pelvis measures only 1.5 by 0.4 cm. at its widest portion and is located eccentrically. There is no demonstrable communication between the renal channels and the cyst which is a closed space and is completely invested by renal capsule. The hilar vessels are small and sclerotic (figs. 2 and 3).

"Sections of kidney reveal very marked fibroid thickening of the capsule. The thickened capsule has laminations of old, hyaline connective tissue, in which are a few deposits of calcium salts. Other portions of the thickened capsule contain many small vessels associated with young connective tissue cells. Some portions also show nodular infiltrations of lymphocytes and there are a few areas which stain very light pink, indicating crystoid change with dilution of protein or a change in its physico-chemical composition. The thickened hyaline capsule is convoluted and forms the wall of the cavity noted grossly. The kidney proper is not remarkable except for some small, old infarcts with lymphocytic infiltration and localized subcapsular edema of some of the glomeruli. Some portions also show foci of tubular regeneration, microscopic in size, in the outer zone of the cortex. There is no neoplasm.

"Hyaline cyst, perirenal. It is impossible to determine the origin or etiology of this lesion. It is quite possible that it is secondary to an old traumatic insult, but an infectious or simple inflamatory lesion could as easily be the causative factor." Signed Harold Gordon, M.D., Chief, Laboratory Services.

The 3 months' postoperative follow-up revealed an asymptomatic patient with a blood pressure of 126/78. He had had no headaches since nephrectomy.

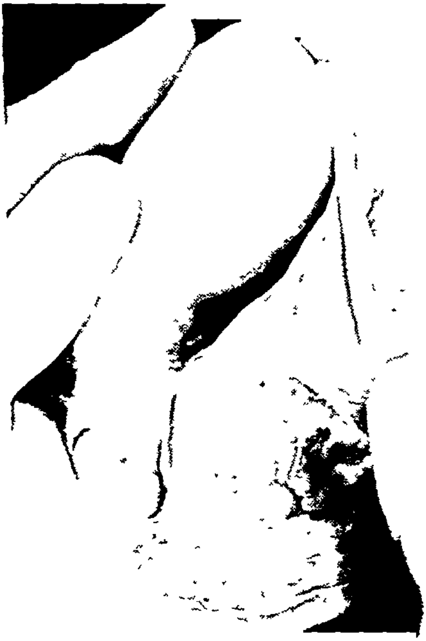

FIG. 2. Showing continuity of cyst with fibrous capsule, also definite lack of continuity with renal cortex.

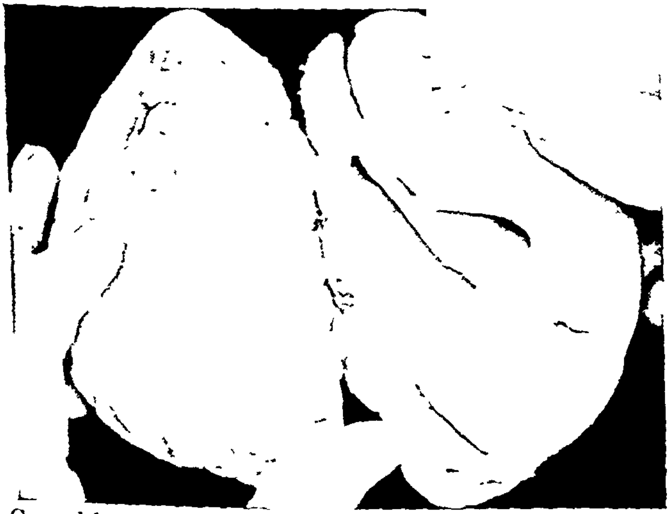

FIG. 3. Coronal hemisection through kidney and perirenal cyst showing cleavage between the two, and demonstrating pressure atrophy of renal substance.

Of some interest is the fact that a preoperative diagnosis of renal neoplasm was made in the previously reported cases and suspected in the case reported here.

At operation there was a definite impression of malignancy. No mention of blood pressure was made in either of the reported cases, and a normal blood pressure is assumed. The moderately elevated blood pressure in the case reported here returned to normal postoperatively and remained well within normal limits at the time of the three months postoperative follow-up.

SUMMARY AND CONCLUSIONS

Perirenal cyst is a rare clinical entity.

Two previously reported cases are reviewed and an additional one reported.

A correct preoperative diagnosis was not made in any of the three cases.

A definite etiological factor was not proved in any of the cases, although trauma is quite probable in at least one case.

There is no characteristic finding of significance, either by history, physical examination or laboratory studies that would aid in a specific diagnosis of this entity preoperatively.

203 W. Second St., Lexington, Ky.

REFERENCES

Baudin, A. and Delclaux, P.: Ann. de Med. Legals, **19**: 648-651, 1939.
Gutierrez, R.: Arch. Surg., **44**: 279-315, 1942.
Shih, H. E. and Wu, S. D.: Chinese Med. J., **59**: 256-258, 1941.

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VESTIGIAL EPIDIDYMAL STRUCTURES IN UNILATERAL RENAL APLASIA

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Anomalies of the genito-urinary tract are extremely common and vary in severity, from the gross deformities, incompatible with life, to the mild normal variants, present in almost every individual, and of no clinical importance. This potential, for frequent and complex developmental anomalies, is readily understood when the embryological development of the genito-urinary tract is considered.

The most primitive of all kidneys, the pronephros, develops first, is not functional in man, and completely disappears early in fetal life. The mesonephros, also a primitive kidney, develops but is not functional, although certain elements persist and enter into the formation of the permanent genito-urinary tract. The excretory duct of the mesonephros, the wolffian duct, persists and enters into the formation of the vas deferens and epididymis. At the fourth week of fetal life, the ureteral bud arises from the dorsal aspect of the wolffian duct and grows cranially to unite with the renal blastema, which develops from an unsegmented, caudally located nephrogenic mass. The permanent kidney, or metanephros, is formed from the ureteral bud, as are the ureter, kidney pelvis and collecting tubules. From the renal blastema, develop secretory elements of the kidney. For development of the renal blastema, a contact must be made with the cranially growing ureteral bud. Failure of the union to take place results in renal aplasia or failure of the kidney to develop. The ureter and kidney pelvis may be arrested in various phases of their development. The mass, capping the tip of the ureter, in such an instance, is not a kidney and does not contain glomeruli or the more proximal tubules of the nephron. Collecting tubules may be present in the mass and have their origin from the ureteral bud. If, on the other hand, there is union of the ureter with the renal blastema, but development fails to take place, a rudimentary kidney is formed, and the aplastic kidney thus formed may contain glomeruli and tubules in varying quantities.

A case of renal aplasia, with contained remnants of the wolffian duct and other interesting features, is presented for record and for its diagnostic and therapeutic significance:

CASE REPORT

W.C.T., No. 66 026, a 30 year old, white bus driver was first admitted to this Veterans Hospital, July 13, 1948. He gave a history of backache of 3 years' duration with intermittent hematuria. He had bouts of backache and hematuria while in the service and cystoscopy was performed several times. A diagnosis of con-

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Sponsored by the VA and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are a result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

genital absence of the left kidney and left ureter with a ureteral diverticulum was made and the patient had been given a medical discharge for "pus in his urine." He was also treated for syphilis and epididymitis while he was in serivce. An excretory urogram and a retrograde pyelogram done at this hospital revealed a normal right kidney and absence of the left kidney. Cultures made of the urine from the right kidney showed growth of Streptococcus fecalis. Cystoscopy revealed that the right side of the bladder was normal but no left ureteral orifice could be seen. A diverticulum 2 cm. in diameter was noted, overlying the probable location of the left ureteral orifice. A catheter passed into this diverticulum could not be made to pass into a left ureter. The patient developed acute otitis media and pharyngitis and when he recovered, he left the hospital.

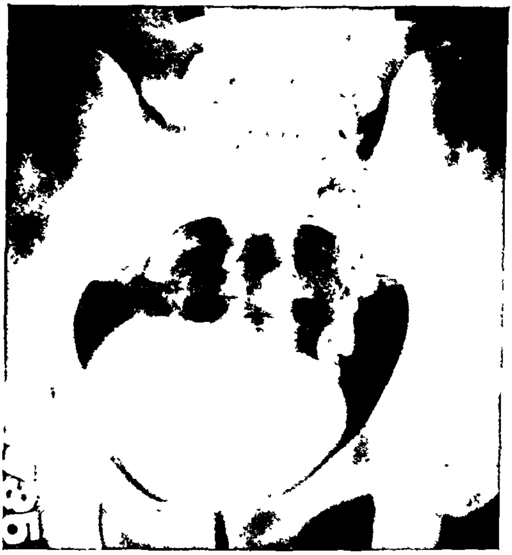

FIG. 1. Cystogram, including lower abdomen, shows bladder greatly distended with opaque substance. Irregular shadow above left upper quadrant. Patient instructed to strain, and this filled up showing tortuous tubular structure up to second lumbar vertebra. Outline of right kidney alone is seen. Lateral film shows this tortuous structure outline up to second lumbar vertebra.

A year later, the patient presented himself with an aggravation of his previous hospital admission complaint. A physical examination at this later admission revealed nothing of significance except as related to the genito-urinary system. Of particular note is the fact that both testicles and both epididymides were normal in size, shape and position. A urethral stricture, noted at time of previous hospitalization here, was present but easily dilated. The prostate was bilaterally enlarged, grade 1, firm, but nontender and smooth. A cystogram, including the whole of the abdomen, showed the bladder to be greatly distended with the iodide solution (fig. 1). There was an irregular shadow extending above the left upper quadrant of the bladder. The patient was instructed to strain and the shadow filled, revealing a tortuous ureteral structure up to the level of the second lumbar vertebra. The outline of the right kidney alone was seen. X-ray examination of the heart and lungs revealed no abnormality. A repetition of the excretory urogram gave the same findings as described for a similar examination at the first admission to this hospital. Complete blood counts were within normal limits. Repeatedly, the urinalysis showed albumin 1 plus and 18 to 20 white blood cells and an occasional red blood cell per high power field. The bleeding time was 2 minutes and the coagulation time 5 minutes. The Kahn test negative.

Operation (Dr. B. S. C.): At operation, the distal segment of the left ureter was approached through a modified Gibson incision. The ureter was divided near the bladder and the distal orifice closed by inversion. The ureter was found to be markedly thickened but not unduly indurated. It was very tortuous. The patient was then turned on his right side and the ureter approached through a classical lumbar incision. The divided end of the left ureter was picked up and the ureter traced upward into the renal fossa. Here a mass, with the absence of Gerota's fascia, was palpated at the end of the ureter. This mass was not completely identifiable as a kidney. No renal pedicle could be found; consequently, a block removal of the mass was performed. Grossly, the specimen seemed to be comprised of fibrous tissue. There was no true renal capsule, but the perinephritic fat was closely adherent to the mass. A wooden applicator inserted in an incision in the ureter was seen to emerge in the middle of the fibrous mass.

FIG. 2. Gross specimen. No renal capsule, and perinephritic fat was closely adherent to this mass.

The convalescence was uneventful. A recheck cystogram at the end of twelve days revealed a smooth bladder outline and the absence of the left ureter.

Pathological examination (Dr. E. S. Cardwell, Jr.): The kidney, a large amount of adjacent fat tissue, and the ureter, weighed 51 gm. The kidney measured 2.7 by 2 cm. It was composed of firm, elliptical, white tissue. The capsule could not be identified and the kidney tissue was not sharply defined from the adjacent adipose tissue. The cortex and medulla were blended to form a mass of elastic

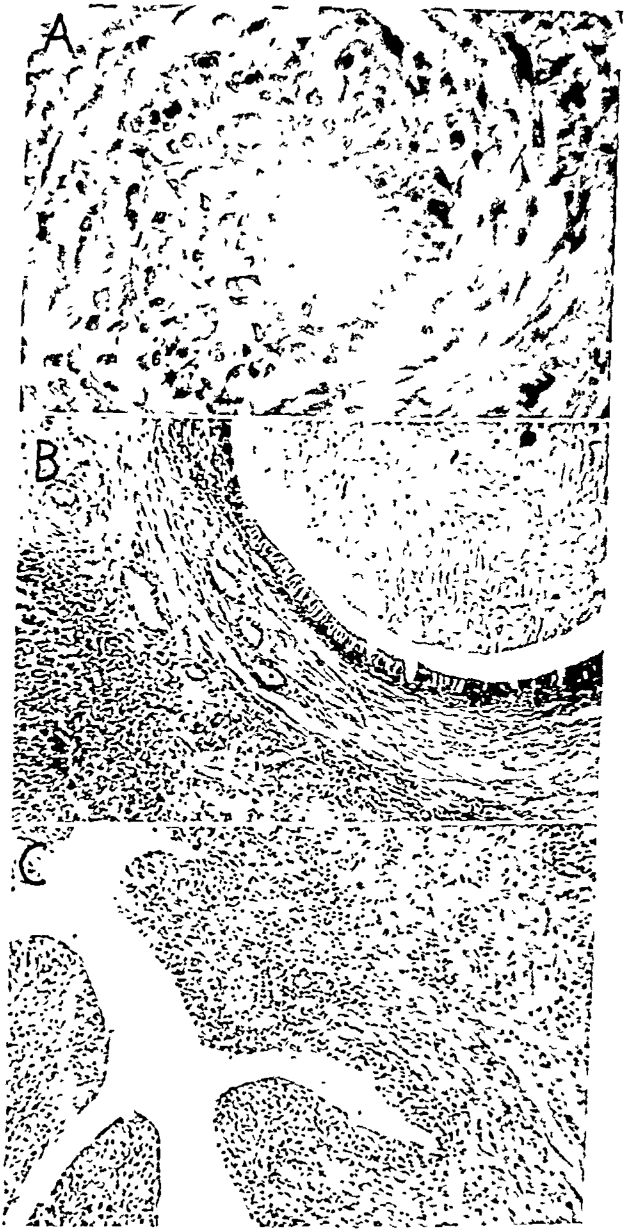

FIG. 3. *A*, glomerulus *B*, ciliated columnar epithelial cells, similar to epididymal tubules, surrounded by smooth muscle, lying in excised renal mass. *C*, round cell infiltration of ureteral wall.

white tissue in which there were islands of fat. The pelvis was presented only by a slit-like space 0.7 cm. long and 0.2 cm. wide. A section of the ureter 20 cm. long was attached. It was very tortuous and up to 0.8 cm. in diameter. See figure 2. On section there was pronounced thickening of the ureteral walls. In the lower pole, the lumen was narrow, while in the upper pole, the walls were slightly dilated and the walls were thinner.

Microscopic examination of sections: The structure which was described as kidney was composed of fibrous connective and adipose tissue. Throughout there was a very dense lymphocytic infiltration which was irregularly distributed. Only very rare foreign body giant cells were seen and in one area there was a small focus of calcification but three glomeruli, all partly fibrosed, were seen in two entire microscopic sections. Scattered throughout the sections were numerous tubular structures lined by epithelial cells. A few of these were lined by fattened epithelium and resemble connecting tubules. Most of the tubules, however, were large and surrounded by a thick layer of smooth muscle. These latter tubules were lined by a double layer of epithelium of which the cells toward the lumen were tall, columnar and had oval nuclei and some of these cells were ciliated. Beneath the inner layer of cells there was a second layer of poorly outlined polyhedral cells which had small, rounded, or slightly oval nuclei. An occasional slightly thickened, small artery was observed in the sections. The kidney pelvis was lined by transitional epithelium beneath which there was a dense, irregular lymphocytic infiltration with the formation of germinal lymphoid follicles. There were several minute collections of epitheloid cells surrounded by a dense ring of lymphocytes in the center of which there was a small foreign body giant cell. The ureter was lined by transitional epithelium beneath which there was also a slight round cell infiltration. The muscular coat was thickened by fibrous connective tissue. The abnormal appearance of the kidney was apparently on the basis of a congenital aplasia of a portion of the wolffian body. Many of the tubular structures seen in the sections were similar in appearance to the tubules which formed in the epididymis. Inflammatory changes were not specific. Diagnosis: 1) Congenital abnormality of the kidney; 2) pyelonephritis, chronic; 3) ureteritis, chronic. See figure 3.

SUMMARY

A case of unilateral renal aplasia which contained vestigial remains of epididymal tubules is reported. Of utmost importance is that normal testicles and epididymides were found in normal position on physical examination. As far as could be traced, the vas deferens seemed to be normal bilaterally. The presence of a dilated, tortuous ureter, and an unidentifiable mass at L-2 was found on voiding cystogram. An excretory urogram revealed the absence of the left kidney. (Cystoscopy failed to reveal the left ureteral orifice.) Surgical approach was first made through a modified Gibson incision and the vesical end of the ureter was freed and divided at the bladder level, with repair of the diverticulum The ureter was traced proximally to the unidentified mass in the renal fossa, which was then approached through a small flank incision, obviating the neces-

sity for the usual long mutilating classical kidney and ureter incision. Patient made an uneventful postoperative recovery. Recheck voiding cystogram showed the left ureter to have been completely removed and the diverticulum absent.

4223 Colonial Park Drive, Pittsburgh 27, Pa. (*F. E. C.*)

REFERENCES

Ainsworth, T.: South. Med. J., **29**: 619, 1936.
Collins, D. C.: Ann. Surg., **95**: 715, 1932.
Edisendrath, D. N.: J. Urol., **33**: 331, 1935.
Hawes, G. A.: J. Urol., **42**: 500, 1939.
Hawthorne, A. B.: Am. J. Surg., **3**: 37, 1927.
Herbst, R. H.: Surg., Gynec. & Obst., **61**: 306, 1935.
Houle, L. B.: Personal communications.
Karol, H. J.: Personal communications.
Mallard, R. S.: J. Urol., **46**: 216, 1941.
Pohlman, A. G.: Johns Hopkins Hosp. Bull., **16**: 51, 1905.

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INTRAPELVIC FIBROMA

SIDNEY IMMERGUT AND ZACHARY R. COTTLER

Malignant growths of the renal pelvis are comparatively rare, their reported incidence ranging from 5 to 10 per cent of all renal neoplasms. Benign lesions, however, are truly rare, especially histoid growths. Many so-called papillomas have been reported, but since they were diagnosed after nephrectomy, their clinical course could not be followed, and it cannot be accurately stated that they are truly benign. Our search of the recent literature revealed but one case, reported by Boross in 1929, that corresponds to ours.

CASE REPORT

R. P., a white woman, aged 32, consulted us on July 11, 1949. She stated that 10 days previously she had an episode of sharp pain in her right side. This persisted for 3 days and disappeared following the onset of hematuria, with clots, and marked frequency and uregency. Approximately $1\frac{1}{2}$ years ago, she had one episode of hematuria, also associated with pain in the right lower quadrant.

Physical examination disclosed no palpable abdominal masses or areas of tenderness. Urine obtained by catheterization was grossly bloody. A flat film of the abdomen did not reveal any opaque calculi.

Immediate cystoscopy was performed. After the evacuation of a considerable quantity of bloody urine and clots from the bladder, clots were seen being extruded from the right ureteral orifice. The left ureteral opening and the bladder mucosa were essentially normal. A catheter was passed to the right renal pelvis and a hydronephrosis of 40 cc bloody urine aspirated. A retrograde pyelogram demonstrated a markedly dilated renal pelvis with numerous filling defects.

The patient was immediately hospitalized. The blood pressure was 118/70, pulse 96 and respirations 20. Blood studies showed the following: Hemoglobin 85 per cent, red blood cells 4.38 million, white blood cells 7,100, polymorphonuclears 50 per cent, band forms 2 per cent, lymphocytes 47 per cent, eosinophils 1 per cent. The following day the hematuria ceased. An excretory urogram made on July 13 showed a normal left kidney and a mottled dilated pelvis on the right, the mottling being possibly due to retained blood clots. The next day menstruation ensued. The patient felt well. A catheterized specimen of urine revealed but a few pus cells. She was discharged, at her own insistence, to be readmitted a week later for further studies.

However, she did not return to the office until March 11, 1950, a lapse of 9 months. Urinalysis revealed: Specific gravity 1.027, pH 6, albumin faint trace, 4–5 pus cells per high power field. Excretory urography revealed a large right renal pelvis with a definite filling defect (fig. 1). Cystoscopy was repeated, revealing a normal bladder, but retrograde pyelography was not done. A diagnosis of papillary neoplasm of the renal pelvis was made and operation advised. Another excretory urogram made on March 30, at the request of a consultant, confirmed the findings of the previous one. The patient was readmitted on April 12.

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Blood studies were essentially the same as previously. The blood urea nitrogen was 16 mg. per cent, blood sugar 82 mg. per cent.

A complete right nephro-ureterectomy was planned utilizing 2 incisions with exploration of the kidney as the first step. We were still skeptical of the diagnosis of a papillary carcinoma. On April 13, 1950, under endotracheal cyclopropane anesthesia, through a curved right loin incision, the kidney was exposed. The kidney and ureter were essentially normal but the pelvis was markedly dilated and contained a firm, semisolid mass. Nephrectomy was performed, including the proximal 4 inches of ureter. While we closed the wound, the pathologist opened the specimen and pronounced the lesion to be benign grossly. The contemplated second stage ureterectomy was therefore deferred pending the microscopic examination of the tissue. Convalescence was uneventful. The ureterectomy was not necessary and the patient discharged from the hospital on April 22, 1950.

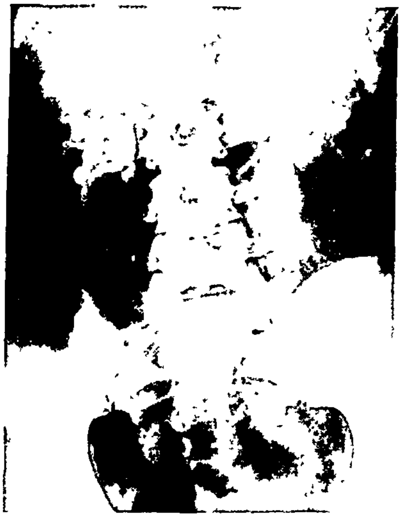

FIG. 1. Excretory urogram. Dilatation of right renal pelvis with mottled filling defect.

Pathological report (Dr. D. M. Grayzel): The gross specimen consisted of a total right kidney measuring 9 by 5 by 4 cm. and weighing 130 gm. The capsule stripped with ease revealing a pink tan, smooth surface. The pelvis was dilated and contained a firm mass within it. The attached portion of ureter was not remarkable. The cut surface of the kidney revealed the cortex to measure 0.6 cm.; it was yellowish tan and clearly differentiated from the medulla which was pinkish tan and measured 1.3 cm. in thickness.

Attached to the pelvic mucosa by a thin pedicle there was a markedly edematous, smooth, pink, lobulated mass measuring 7 cm. in length and 1.5 cm. in thickness. The remainder of the pelvic mucosa was gray white, smooth and glistening (fig. 2).

Microscopic: The tumor consisted of widely separated collagenous fibers in a pink staining homogeneous matrix. The latter contained a moderate number of

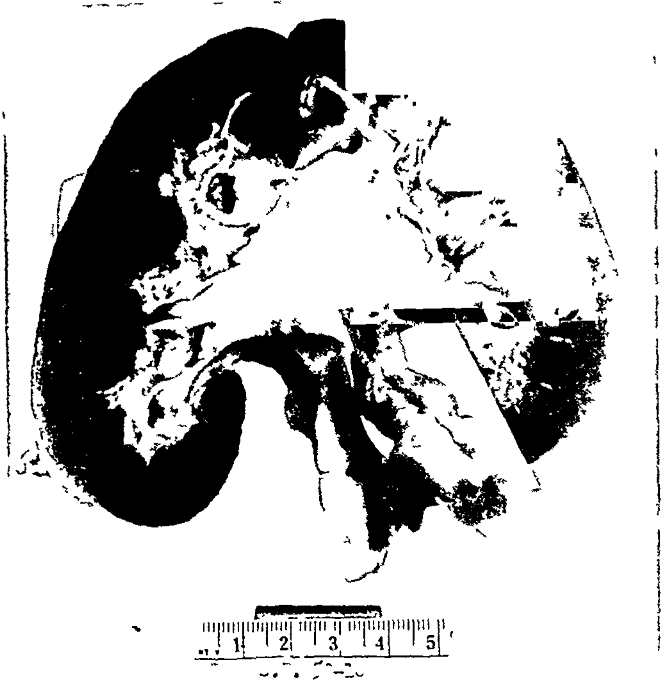

FIG 2 Gross specimen Large edematous pedunculated polypoid mass arising from medial pelvic wall, just proximal to the ureteropelvic junction

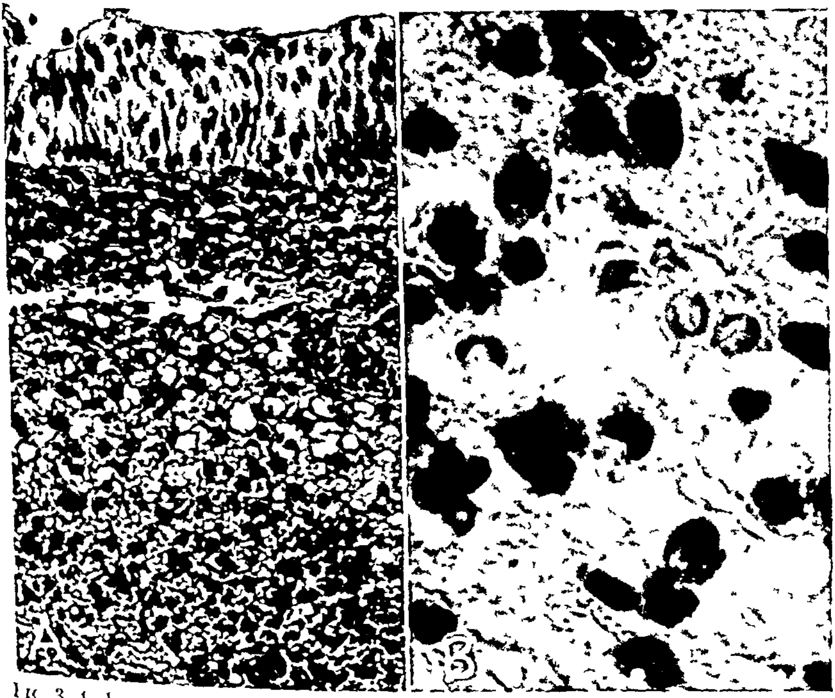

FIG 3 A, demonstrating cellular infiltration in colloidal matrix Surface of tumor lined by typical urothelium × 150 B, demonstrating homogeneous colloidal matrix eosinophiles and round cells × 150

fibroblasts, eosinophils and small round cells. The surface was lined by urothelium of usual thickness. The renal parenchyma and ureter revealed no features of note (fig. 3). Diagnosis: Polypoid edematous fibroma of renal pelvis.

DISCUSSION

Fibromas of the ureter have been reported on several occasions (we are preparing a report of a case), but other than Boross' case, none have been reported as originating in the renal pelvis.

The clinical, roentgenological and urological features of the lesion parallel those of papillary carcinoma, without ureteral or vesical implants, and the so-called benign papilloma of the renal pelvis.

The remarkable feature was the severe hematuria which spontaneously ceased. Our explanation of this phenomenon is based on the thin pedicle attaching the mass to the pelvis. We believe that some degree of torsion of the pedicle must have occurred, similar to the torsion of the testicle, resulting in venous stasis, infarction, rupture of vessels and subsequent hematuria. The edematous character of the mass strongly supports our hypothesis.

The diagnosis of a benign lesion can only be made at the time of operation. Although these tumors are the rare exception, we prefer, in doubtful cases, to do the renal part of a total nephro-ureterectomy as the first step. Thus the patient can be spared an unnecessary procedure and the longer convalescence.

SUMMARY

A case of fibroma of the renal pelvis is presented, the second in the literature to our knowledge.

An explanation for the one and outstanding symptom, hematuria, is proffered, torsion of the pedicle of the mass.

4711 Twelfth Ave., Brooklyn 19, N. Y.

REFERENCES

Boross, E.: Fibroma of renal pelvis. Orvosi hetil, 73: 1055, 1929.
Cabot, H.: Modern Urology. Philadelphia, Lea & Febiger, 1936.

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A NYLON THREAD URETERAL STONE EXTRACTOR

PAUL L. SINGER

The chief objections to the Ellik looped catheter ureteral stone extractor are: A relatively large catheter is required which in being passed beyond the stone presents a whistle tip point as well as a loop of steel wire towards the stone; twisting of the catheter must be avoided; a large renal pelvis is needed to form the loop; and in the downward passage a double thickness of catheter besides the stone must traverse the ureter.

An ideal catheter stone remover should have a small caliber with a filiform or olive tip as the sole presenting point to the stone; it should not need to go up to the renal pelvis to form a loop; the size or shape of the pelvis should not be a consideration; and the stone alone should be required to pass down the ureter.

These requirements being kept in mind the following loop was devised. A No. 4 olive tip catheter is used. This is threaded with 120 cm. length of nylon thread (Zytor No. 0) starting with an eye furthermost from the olive tip and passing it retrograde until the thread projects at the cut end for 10 cm. A knot is here made in the thread. The remaining length of thread is folded back along the catheter from the eye down, and the loop is ready for use. It is passed through an ordinary cystoscope and maneuvered past the stone as far as it can go. No care is taken to avoid twisting the catheter. Once the catheter is well above the stone, it is twisted several times, and the catheter is gently withdrawn until the tip is in the bladder. This maneuver permits the outside thread to lie alongside the stone with the loop well above the stone. The two ends of the thread are then grasped in one hand, and gentle traction is made so that the loop catches on a sharp projection of the stone and is slowly drawn into the bladder. If the stone slips during the procedure another one may be passed since trauma is minimal with the small catheter. Occasionally the loop will cut the stone (3 cases) into two fragments.

This loop has been used by me for the past year exclusively on all cases where passage beyond the stone was possible. There were 23 such cases. The stone was delivered at the first sitting in 14 cases. In 5 cases repeated attempts failed, but the stone was pulled down somewhat and passed subsequently. The other four cases required open ureterotomy.

The loop has also been used with success on several occasions by Dr. Robert H. Cummings of this city.

I believe that the loop deserves a trial on an extensive scale, especially, since it is a less traumatizing procedure.

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OBSERVATIONS ON THE DYNAMICS OF ACUTE URINARY RETENTION IN THE DOG

JOHN D. LAWSON AND WM. B. TOMLINSON

From the Harrison Department of Surgical Research, School of Medicine, University of Pennsylvania and the Philadelphia General Hospital, Philadelphia, Pa.

In 1903, Kelling during a study of the physical properties of rubber balloons noted that inflation of a spherical balloon produced an early rapid rise in pressure to a peak which was followed by a gradual decrease in pressure for a prolonged interval, and then a rapid decline of pressure just before rupture of the balloon. In 1909 Osborne carried out somewhat similar experiments upon rubber balloons and extirpated canine bladders and reported similar results.

In 1948 Brody and Quigley supplied the necessary mathematical explanations to explain such a phenomenon. They developed an equation which seems accurately to express the pressures developed within a hollow, perfectly elastic sphere during distention. They postulated that such mechanical factors may play a part in the distention characteristics of certain hollow viscera in vivo, and that they may be partly responsible for such phenomena as 'receptive relaxation.'

With this background we decided to determine the bladder pressure-distention curves in dogs during acute urinary retention.

METHOD

A group of mongrel dogs were anesthetized with sodium pentothal in doses which were designated to maintain them in as light a level of anesthesia as possible. During the entire experiment they received a constant intravenous infusion of 2.5 per cent glucose in distilled water at such a rate that at the end of 36 hours they received a total of 1500 to 2000 cc of fluid. Once anesthetized, the dogs were catheterized with a No. 16 Foley catheter which was connected to a water manometer.

RESULTS

The results of acute urinary retention in these dogs is shown by the following representative curves.

It will be seen in figure 1, *A* that the bladder pressure increased to a peak in 12–18 hours and then slowly declined to rather low pressure levels. These curves are approximately those one would theoretically expect.

The pressure-distention curves of dogs subjected to rapid filling of the urinary bladder with 500 cc physiologic saline over a period of 19 minutes were determined in order to ascertain the effect of the time of filling on the curve characteristics of the normal bladder.

As is seen in figure 1, *B*, the pressures rise rapidly to a sustained plateau which is maintained until a total of 500 cc has been added. For a 10 minute period immediately following the installation of 500 cc physiological saline solution there was a drop in pressure to levels of about one-half the plateau pressure although no saline was being added or removed. Interestingly enough, although

500 cc saline was introduced into the dog's bladder, only 380 cc were removed from the bladder while approximately 100 cc clear fluid was recovered from the peritoneal cavity at the conclusion of the experiment. Additional experiments produced similar results. The experiments were repeated with the addition of methylene blue to the distending fluid, so as to provide information on the site of fluid loss. It was found that the fluid was escaping into the peritoneal cavity through the grossly intact bladder wall. No reflux up the ureters was demonstrated even though the ureters were divided near the bladder at the height of distention.

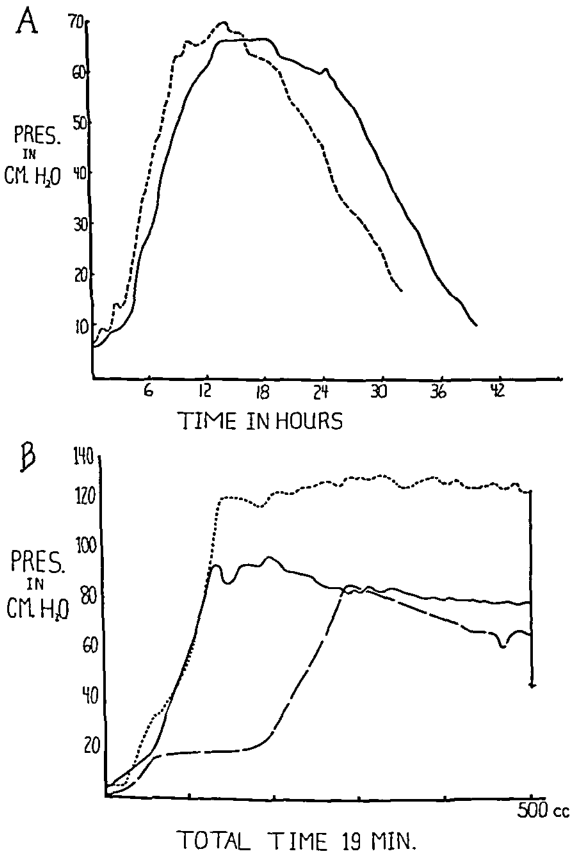

Figure 1

We determined the effect on the type of curve produced of altering the stretch characteristics of the bladder. This was accomplished by repeated rapid distention of a dog's urinary bladder to approximately 500 cc capacity, with the production of submucosal hemorrhages and thromboses. During the following weeks the bladder became somewhat contracted and fibrotic. Although the bladder had been subjected to this trauma, there was no subsequent clinical evidence of

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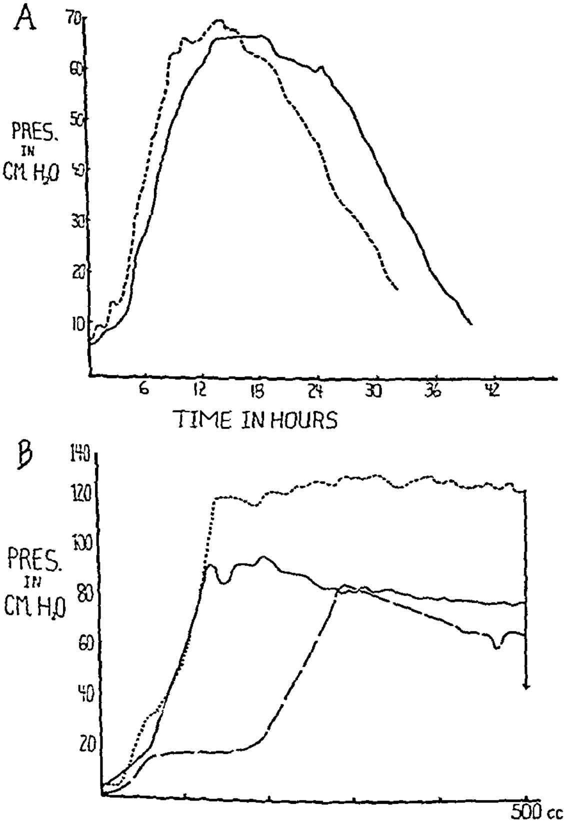

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We determined the effect on the type of curve produced of altering the stretch characteristics of the bladder. This was *accomplished by repeated rapid distention* of a dog's urinary bladder to approximately 500 cc capacity, with the production of submucosal hemorrhages and thromboses. During the following weeks the bladder became somewhat contracted and fibrotic. Although the bladder had been subjected to this trauma, there was no subsequent clinical evidence of urinary dysfunction such as incontinence, frequency or discernible evidence of pain.

As will be seen in figure 2, when a dog with a fibrotic bladder experiences acute urinary retention, the curve produced differs markedly from the distention curves of normal canine bladders (figure 1, *A*) in the following respects: 1) The initial rise of bladder pressure is much more abrupt. 2) There is no sustained fall in pressure following a peak, but rather, the pressure continues to rise to a very high level followed by rupture of the bladder, a circumstance which does not occur in normal bladders.

It is obvious that this type of preparation is almost ideal for determining the secretory pressures of the dog's kidneys because there is no instrumentation of the ureters and the only trauma involved is the insertion of the urethral catheter. The high bladder pressure obtained could be due only to the secretory pressure of the dog's kidneys because, as has been shown by Trattner ureteral peristalsis stops at ureteral pressures of 54.0 cm. of water.

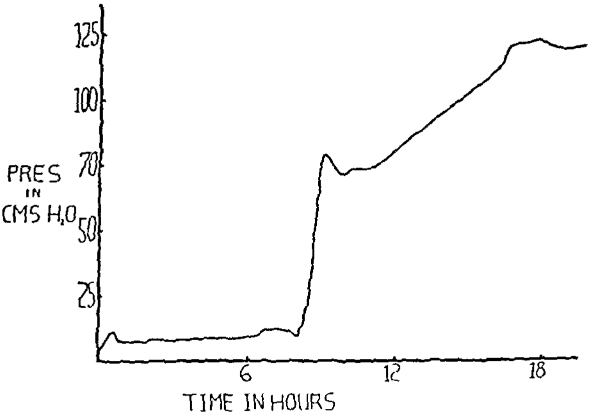

Figure 2

Other investigators* have found lower secretory pressures by directly connecting the proximal ureter to a recording manometer, but they were handicapped by evidence of some type of backflow. The operative trauma may also have had some effect on their results. Our results do compare favorably with the pressures obtained by Rolnick and Singer who found that the secretory pressures were about 133 cm. of water. The highest pressure observed by us was 126 cm. of water. We believe that the value of 126 cm. of water pressure is somewhere near the peak of secretory pressure of the dog's kidney. This problem is being further investigated.

Since the normal dogs in acute urinary retention developed 100-150 cc fluid in the peritoneal cavity, the question of prime importance became whether or not the fall in bladder pressure following the peak was due to interstitial leakage through the bladder wall into the peritoneal cavity or due primarily to the physical stretch characteristics of the bladder.

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* Barney, Guyon, Jones.

In order to determine the origin of the free peritoneal fluid simultaneous samples of bladder urine, blood and peritoneal fluid were examined for their respective contents of urea. In every instance the blood urea nitrogen and the peritoneal fluid urea nitrogen were found to be identical; whereas the bladder urine urea nitrogen was found to be concentrated about 13–15 times the values in the other specimens. Also since the peritoneal fluid was blood tinged and showed evidence of clotting, it was clear that the peritoneal fluid was not coming from within the bladder, but most probably from the rupture of small subserosal bladder vessels. The fact that methylene blue passed through the bladder wall during rapid distention and not in slower acute urinary retention would indicate that there was more disruption of bladder components in the rapid distention and that the rate of distention, rather than the final volume of urine was the determining factor in the leakage of urine from the bladder into the peritoneal cavity.

Another question of importance seemed to be whether or not a bladder would follow the same type of curve which had previously been produced during acute urinary retention (fig. 1, A) if the dog's own urine were dripped into his bladder at a *constant* rate.

Preparation for this experiment consisted of isolating both kidneys and ureters retroperitoneally, tying the ureters near the bladder, and leading the free ends of the open ureters to the outside. The urine was then collected from these free ends and siphoned at a constant rate into the dog's own bladder.

As can be seen in figure 5A, the pressure rose precipitously and then came down as it did in the previous experiments. During the 25 hours in which the dog was studied a total of 437 cc urine was placed in the bladder, but only 350 cc urine could be removed. This left an unexplained deficit of 87.0 cc urine. Again urea analyses were made as described previously with the following results: blood urea nitrogen = 50.0 mg. per cent: peritoneal urea nitrogen = 160 mg. per cent and urine urea nitrogen = 550 mg. per cent. This data would suggest that there was a leakage of urine into the peritoneal cavity.

Other findings of significance were: 1) Absence of ureteral dilitation below the ligatures; 2) production of submucosal hemorrhages in the bladder, principally in the posterior superior portion of the dome; 3) absence of pathologic changes in the tissues adjacent to the catheter or Foley bag; 4) when the dog finally expired the final pressure was observed for 15 minutes with no change; upon the slow addition of 3.0 cc urine to the bladder the bladder pressure decreased about 1.0 cm. and was thereafter constant. This is most probably explained on a purely mechanical basis and could not logically be explained on the basis of extravasation of bladder urine at this point.

Finally it is interesting to note that the dog's urinary output became so reduced as distention proceeded that urine which was collected previously had to be supplemented to maintain a constant rate of inflow whether or not this was due to reflexes set up in the distended bladder we are unable to state at this time, although it is highly possible that bladder distention in some way caused oliguria. This is very interesting because there was no mechanical connection between the bladder and the kidneys which became oliguric during distention.

We then determined the relation between the bladder pressures and renal pelvis pressures during acute urinary retention. The preparation consisted of isolating both kidneys and ureters retroperitoneally. T tubes were then inserted into the ureters about one-half cm. below the renal pelvis. Pressures were then recorded simultaneously from both renal pelves and from the urinary bladder.

During the first 8 hours (fig. 3), there were sharp intermittent increases and decreases of the pelvic pressures which were accompanied by mild changes in bladder pressure. The changes in pelvic pressure may be due to: 1) pyelovenous or pyelo-interstitial backflow; 2) spasm of the ureters due to the operative procedure; 3) lack of ureteral peristalsis due to interruption of the continuity of the ureters with or without urinary backflow. Following this state, the pelvic pressure of one kidney paralleled the bladder pressure while the opposite pelvic pressure continued to fluctuate at a low level.

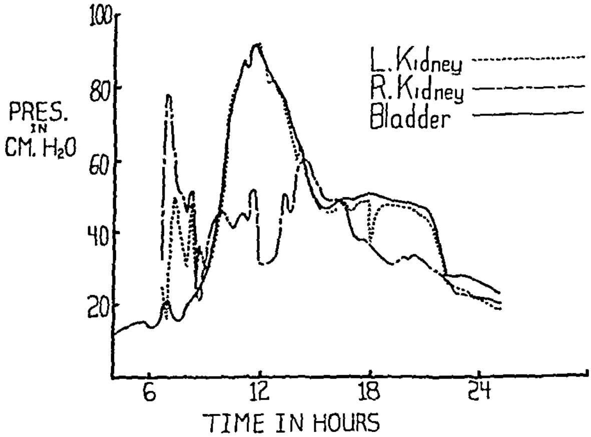

Figure 3

We then determined the pelvic pressure of an isolated kidney while the bladder was being distended by the function of the opposite kidney. The dog was prepared by isolating one kidney and connecting its pelvis directly to a manometer, the distal portion of the ureter near the bladder being tied. The bladder was distended by the functional activity of the opposite kidney.

The ureteral pressure (fig. 4, broken line) rose abruptly to about 50.0 cm. of water pressure and then showed sharp intermittent fluctuations of pressure. We believe that these fluctuations of pressure could be explained only by some type of kidney or pelvic backflow because: 1) The pelvic and calyceal capacity was 1.0–2.0 cc. 2) The volume of urine necessary to record these changes in the manometer was of the order of 2.0–4.0 cc. 3) There was no transpelvic or extrarenal leakage during these changes. 4) The pressure changes were rapid. Hence the avenue of escape must be venous, lymphatic, interstitial, or resorptive.

Following the initial fluctuations described above, the pelvic pressure mirrored the bladder pressure at a lower level of pressure even to variations as slight as

3.0 cm. of water pressure. This is difficult to understand in view of the absence of any mechanical connection between the two systems.

Finally, we present a composite graph which we believe probably represents the importance of a decrease in rate of urinary output with an increase in bladder or pelvic pressure. As will be seen in figure 5, *A*, when a normal bladder is filled at a *constant* rate based on the volume found in a normal bladder during a comparable time interval, the bladder pressure rises to a very high level. With such high bladder pressure extravasation of urine into the peritoneal cavity occurs; whereas, in acute urinary retention (fig. 5, *C*), a decrease in the rate of urine output at the peak enables the bladder to accommodate a comparable volume of urine without a comparable rise in bladder pressure with its accompanying extravasation of urine.

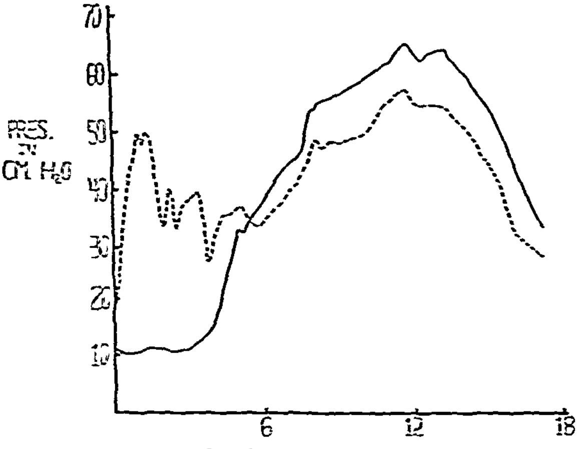

Figure 4

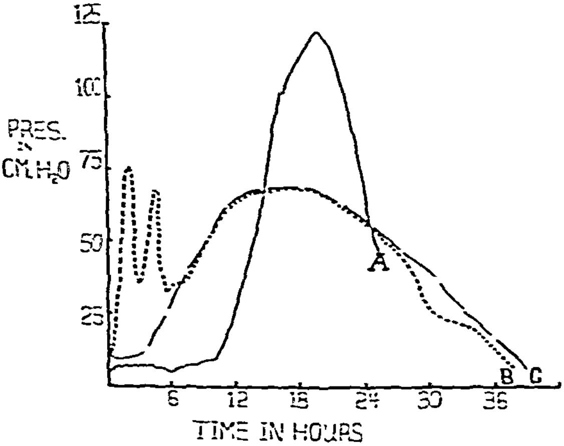

Figure 5

The decrease in urine formation with an increase in bladder pressure may be explained in one of several ways. As may be seen in figure 5, *B*, the pelvic pressure increases with an increase in bladder pressure; this increase in pelvic, and therefore intranephric, pressure results in a decrease in urine flow as shown by the investigations of several authors.* Another possible mechanism which came to light during these experiments was a decrease in urine flow from mechanically isolated kidneys during distention of the dog's bladder which may represent a reflex oliguria secondary to bladder distention. However, this observation has not been adequately substantiated by a sufficient number of observations to warrant its assumption as a constant occurrence. There are a number of investigators†, who believe that pain, or trauma involving the bladder or other viscera may reflexly cause oliguria.

SUMMARY AND CONCLUSIONS

A method is presented which enables one simultaneously to determine the pressures which obtain in different parts of the urinary tract under varying conditions.

During acute urinary retention the pressure within the dog's bladder increases to a peak and then progressively decreases although the volume of the bladder is constantly increasing.

Exogenous filling of a dog's bladder at a very slow constant rate results in abnormally high bladder pressure with resultant extravasation of urine into the peritoneal cavity without a gross disturbance of bladder continuity, after which the bladder pressure decreases as it does in the normal bladder.

Urinary output decreases as intranephric pressure increases during acute urinary retention, which could account for the normally low peak bladder pressures which occur during acute urinary retention. Another explanation for the oliguria may be that it is caused reflexly as a result of distention of the bladder.

Rapid distention of a dog's bladder at a rate of 19.0 cc per minute to a total of 500 cc results in extravasation of a portion of the distending fluid into the peritoneal cavity although no gross break in bladder continuity is observed.

Blood tinged free peritoneal fluid is produced in every case of prolonged acute urinary retention.

A method is given for experimentally producing a fibrotic urinary bladder which is of some experimental interest especially in the determination of the secretory pressure of the kidney.

Acute urinary retention of great degree causes submucosal hemorrhages and thromboses with the formation of blood tinged urine. The dome of the bladder appears to be the site of predilection for these hemorrhagic phenomena.

In every case of acute urinary retention within 24–36 hours bilateral hydroureter, hydropelvis, and moderate hydrocalyx develop.

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* Brodie + Cullis; Heidenhain; Henderson; Ludwig; Peters; Theobold and Verney; Winton (1931); Winton (1937).

† Black and Saunders; Gardner and Fox; Goodwin, Sloan and Scott; Trueta, Barclay, Daniel, Franklin and Prichard.

In these dogs no instance was encountered at any level of pressure at which there was evidence of incompetency of the ureterovesical junction.

Attempts to arrive at an effective modulus of stretch for smooth muscle of the bladder, or the bladder as a whole cannot be used reliably in physiological work since the rate of distention is a determining factor in the type of curve produced.

The secretory pressure of the dog's kidney is approximately 126 cm. of water.

REFERENCES

Barney, J. D.: Trans. Am. Assoc. Genito-Urin. Surg., 7: 201, 1912. (Quoted by Rolnick.)
Black, D. A. K. and Saunders, M. G.: Lancet, 256: 733, 1949.
Brodie, T. G. and Cullis, W. C.: J. Physiol., 34: 224, 1906.
Brody, D. A. and Quigley, J. P.: Bull. Math. Biophysics., 10: 25, 1948.
Gardner, W. D. and Fox, C. A.: Anat. Record, 100: 663, 1948.
Goodwin, W. E., Sloan, R. D. and Scott, W. W.: J. Urol., 61: 1010, 1949.
Guyon, F.: Ann. Mal. des Org. Genito-Urin., 10: 161, 1892. (Quoted by Rolnick.)
Heidenhain, R.: Hermann's Hand b.d. Physiol., 5: (i), 1883.
Henderson, U. E.: J. Physiol., 33: 175, 1905.
Jones, W. C.: Am. J. Obst. & Dis. of Women & Children, 70: 329, 1914. (Quoted by Rolnick.)
Kelling, G.: Ztschr. f. Biol., 44: 161, 1903.
Ludwig, C.: Lehrbuch d. Physiol. 1861, 2nd ed.
Osborne, W. A.: Proc. Royal Soc. London (B), 81: 485, 1909.
Peters, J. T.: Ann. Int. Med., 23: 221, 1945.
Rolnick, H. C. and Singer, P. L.: J. Urol., 57: 834, 1947.
Theobold, G. W. and Verney, E. B.: Quart. J. Exper. Physiol., 25: 341, 1935.
Trattner, H. R., Wright, H. B. and Barlow, O. W.: J. Urol., 23: 441, 1930.
Trueta, J., Barclay, A. E., Daniel, P. M., Franklin, K. J., and Prichard, M. M. L.: Studies of the Renal Circulation. Oxford: Blackwell Scientific Publications, 1947.
Winton, F. R.: J. Physiol., 71: 382, 1931.
Winton, F. R.: Physiol. Rev., 17: 408, 1937.
Wolf, G. A., Jr.: Res. Publ. Assoc. Nerv. and Ment. Dis., 23: 358, 1943.
Wolf, G. A., Jr.: Ann. Int. Med., 23: 99, 1945.

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REFERENCES

Barney, J. D.: Trans. Am. Assoc. Genito-Urin. Surg., **7:** 201, 1912. (Quoted by Rolnick.)
Black, D. A. K. and Saunders, M. G.: Lancet, **256:** 733, 1949.
Brodie, T. G. and Cullis, W. C.: J. Physiol., **34:** 224, 1906.
Brody, D. A. and Quigley, J. P.: Bull. Math. Biophysics., **10:** 25, 1948.
Gardner, W. D. and Fox, C. A.: Anat. Record, **100:** 663, 1948.
Goodwin, W. E., Sloan, R. D. and Scott, W. W.: J. Urol., **61:** 1010, 1949.
Guyon, F.: Ann. Mal. des Org. Genito-Urin., **10:** 161, 1892. (Quoted by Rolnick.)
Heidenhain, R.: Hermann's Hand b.d. Physiol., **5:** (i), 1883.
Henderson, U. E.: J. Physiol., **33:** 175, 1905.
Jones, W. C.: Am. J. Obst. & Dis. of Women & Children, **70:** 329, 1914. (Quoted by Rolnick.)
Kelling, G.: Ztschr. f. Biol., **44:** 161, 1903.
Ludwig, C.: Lehrbuch d. Physiol. 1861, 2nd ed.
Osborne, W. A.: Proc. Royal Soc. London (B), **81:** 485, 1909.
Peters, J. T.: Ann. Int. Med., **23:** 221, 1945.
Rolnick, H. C. and Singer, P. L.: J. Urol., **57:** 834, 1947.
Theobold, G. W. and Verney, E. B.: Quart. J. Exper. Physiol., **25:** 341, 1935.
Trattner, H. R., Wright, H. B. and Barlow, O. W.: J. Urol., **23:** 441, 1930.
Trueta, J., Barclay, A. E., Daniel, P. M., Franklin, K. J., and Prichard, M. M. L.: Studies of the Renal Circulation, Oxford: Blackwell Scientific Publications, 1947.
Winton, F. R.: J. Physiol., **71:** 382, 1931.
Winton, F. R.: Physiol. Rev., **17:** 408, 1937.
Wolf, G. A., Jr.: Res. Publ. Assoc. Nerv. and Ment. Dis., **23:** 358, 1943.
Wolf, G. A., Jr.: Ann. Int. Med., **23:** 99, 1945.

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THE ELECTROLYTE DISTURBANCE IN URETEROCOLOSTOMY

MORTON KORENBERG

Transplantation of the ureters into different portions of the bowel in animals or man is accompanied by more or less definite changes in the electrolyte structure of the organism. Transplantation of a single ureter results in no electrolyte disturbance because the kidney on the unoperated side is able to maintain normal electrolyte balance.

The mechanism of the development of these changes in cases of bilateral ureterocolostomy has been variously explained: 1) There may be a loss of sodium from the bowel. 2) Damage to the kidney from back pressure, with or without infection, may impair its function in acid-base control. 3) Acid radicals from the urine may be reabsorbed from the bowel and returned to the plasma. Recently Ferris and Odel[1] have interpreted the changes on the basis of selective reabsorption of the chloride ion from urine stored in the rectum and sigmoid.

Recent experience with such cases has prompted me to suggest that the electrolyte change resulting from bilateral ureteral transplantation is attributable to the reabsorption of *sodium chloride* primarily, with secondary intra- and extracellular electrolyte readjustment. A few pertinent observations from the recent literature will serve to make this hypothesis appear reasonable.

It has been shown that a syndrome resembling diabetes insipidus can be produced in normal dogs by repeated injections of desoxycorticosterone acetate.[2, 3, 4] With the administration of desoxycorticosterone there is progressive increase in fluid intake and urine volume. The addition of sodium chloride to the drinking water of these animals increases the excessive fluid exchange, the magnitude of the exchange being dependent upon the amount of sodium chloride in the diet.[4] The experiments of Mulinos et al.[4] demonstrate very definitely the primacy of thirst over the polyuria which follows. Concomitantly there occur a fall in urine specific gravity, a slight but consistent rise in serum sodium concentration, and a fall in the serum potassium.

When the syndrome is well established, attacks of muscular weakness make their appearance. These attacks of weakness or paralysis can be alleviated by the administration of potassium salts.[5] Although it is difficult to detect a significant disturbance of sodium or potassium *balance* during the gradual development of the syndrome, it has been found that the skeletal muscles of animals dying with paralysis contain large amounts of sodium and less than normal amounts of potassium.[5] These authors have noted that the syndrome of diabetes insipidus is associated with the slightly elevated serum sodium concentration. The muscular weakness results from the disturbance of *intracellular* electrolyte concentration, notably, decrease in potassium and increase in sodium.

Since the protective action of potassium salt administration is independent of the serum sodium concentration, Ferrebee et al.[5] refer to this intracellular

[1] Ferris, D. O. and Odel, H. M.: J. A. M. A., **142:** 634, 1950.

[2] Kuhlmann, D., Ragan, C., Ferrebee, J. W., Atchley, D. W. and Loeb, R. F.: Science, **90:** 496, 1939.

[3] Ragan, C., Ferrebee, J. W., Phyfe, P., Atchley, D. W. and Loeb, R. F.: Am. J. Physiol., **131:** 73, 1940.

[4] Mulinos, M. G., Spingarn, C. L. and Lojkin, M. E.: Am. J. Physiol., **135:** 102, 1941.

[5] Ferrebee, J. W., Parker, D., Carnes, W. H., Gerity, M. K., Atchley, D. W. and Loeb, R. F.: Am. J. Physiol., **135:** 230, 1941.

exchange as *replacement* of potassium by sodium rather than *displacement* of intracellular potassium. In other words, it appears that sodium goes into muscle cells only when potassium comes out.

More recently Gilman et al.[6, 7] have demonstrated that the administration of sodium chloride solution to normal dogs is accompanied by a negative balance of intracellular water (i.e. intracellular dehydration), which in turn results in increased urinary excretion of potassium. The cellular dehydration may result from administration of even hypotonic salt solution, and increases with increasing tonicity of the solution administered. Potassium excretion can be correlated directly with the degree of cellular dehydration.

The symptoms and signs manifest in patients with bilateral ureterocolostomy are markedly similar to those found in the above mentioned experimental animals. All patients complain of a persistent salty taste, with thirst associated with ingestion of excessive amounts of water. This leads to polyuria (which appears as diarrhea). This is followed by fatigue, weakness, anorexia, nausea, and vomiting. The serum sodium concentration is found to be normal or slightly elevated, the blood chloride level is elevated, and the serum potassium level is below normal.

The injection of desoxycorticosterone, the administration of sodium chloride solution, and the performance of bilateral ureterocolostomy have in common the tendency to cause sodium chloride retention in the body.

The sodium chloride that appears in the urine of these patients is partially reabsorbed by the bowel. This reabsorption of sodium chloride from the bowel initiates the tendency to cellular dehydration with increased potassium loss from the cells and increased urinary potassium excretion.[6, 7] The diarrhea tends to accentuate this potassium loss.[8] When rehydration of the cells occurs in accordance with Donnan concepts, the potassium lost from the cells is replaced by sodium.[5] The chloride ion remains in the extracellular water and causes depression of the bicarbonate ion. The latter phenomenon has been demonstrated by Gamble[9] to be characteristic of the organism's preference to maintain electrolytic stability at the expense of acid-base balance. The normal bicarbonate value rests upon the integrity of the entire electrolyte structure. Extension of an anion component, in the present instance, chloride ion, thus results in depression of bicarbonate ion and permits the body to maintain electrolytic balance. This accounts for the presence of the "chloride acidosis" and the low carbon-dioxide combining-power of the blood plasma.

In keeping with the foregoing, the treatment of the disturbance must be directed at: 1) the inhibition of reabsorption of excess sodium chloride (the patient must be encouraged to empty the bowel as frequently as possible); 2) maintenance of a low sodium intake; 3) administration of potassium salts to combat the excessive loss incurred by the frequent emptying of the bowel.

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[6] Mudge, G. H., Ames, A., Foulks, J. and Gilman, A.: Am. J. Physiol., **161:** 151, 1950.

[7] Mudge, G. H., Foulks, J. and Gilman, A.: Am. J. Physiol., **161:** 159, 1950.

[8] Darrow, D. C.: J. Pediat., **28:** 515, 1946.

[9] Gamble, J. L.: Chemical Anatomy, Physiology and Pathology of Extracellular Fluid. A Lecture Syllabus, 1939.

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REGRESSION OF CANCER OF THE URINARY BLADDER FOLLOWING URETERO-INTESTINAL ANASTOMOSIS

CHESTER A. FORT, H. C. HARLIN AND H. D. ATKINSON

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Many papers have been written about the etiology of cancer of the urinary bladder but the exact nature of its growth is still unknown. A recent article by Goldberg covers the literature on this subject and gives an interesting case report.

This is a report of another case of regression of cancer of the urinary bladder following ureterosigmoidostomy.*

CASE REPORT

D. D., a white man aged 55, was admitted to Lawson Veterans Administration Hospital on August 25, 1948, complaining of the presence of bloody urine of 2 years' duration. The onset was sudden, painless, gross hematuria. He consulted a local physician who examined him cystoscopically and stated he had "tumors in the bladder" which he treated by fulguration for 11 months. Four months before discharge, he noticed some hesitancy, dribbling, frequency, and incontinence of urination. He also had nocturia 3 to 4 times and a feeling that he was not able to completely empty his bladder.

After discharge, he went to the Bay Pines Veterans Administration Hospital, where a transurethral removal of a bladder tumor was performed, enabling him to void normally. He was then transferred to Lawson Veterans Administration Hospital for further treatment since it was not possible to remove all of the tumor at the Bay Pines institution. At the time of admission to Lawson the patient did not complain of any genito-urinary symptoms. For the past 2 years, he had suffered with severe hypertension, his systolic pressure at times as high as 200 mm. of mercury. He had symptoms of headaches and dizziness associated with his hypertension.

Physical examination was essentially negative. Rectal examination revealed no enlargement of the prostate gland and no mass could be felt in the region of the urinary bladder. The laboratory findings were all within normal limits.

Cystoscopy of August 30, 1948 revealed a papillomatous growth surrounding the bladder neck and protruding into the internal urethral orifice. Larger growths were present on the right inferior lateral margin of the vesical neck. Retrograde pyelograms and ureterograms taken on August 31 were negative. Cystogram showed a filling defect in the region of the vesical neck, suggesting tumor. A biopsy taken from the tumor mass at this time was reported as papillary carcinoma of the urinary bladder, grade 2 (fig. 1, *A*), and was described as follows:

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* It should be borne in mind that this was a case of multiple, intravesically projecting papillomas without microscopic or other evidence of infiltration. *Editor.*

"The specimen consists of 3 small pieces of irregularly shaped soft white tissue. The largest is 4 mm., the smallest, 2 mm. in diameter. The section shows islands and cords of multi-layered epithelial cells. These are set in a small amount of connective tissue stroma. There is a generally intact basement membrane to most of the epithelium. The blood vessels in the stroma show in a few places a small number of epithelial cells. The epithelial cells are usually palisade in arrangement, but in some areas have lost their polarity and vary considerably in size and shape. There are hyaline inclusion bodies within the cytoplasm of some of the epithelial cells. A moderate number of mitoses is seen."

The patient was prepared for operation in the routine manner, with sulfasuxidine, nonresidue diet, enemas, etc., for five days. On September 17 bilateral ureterosigmoidostomy was done, using Coffey 1 technique. The immediate postoperative course was uneventful and the urinary output was good. Nine days postoperatively, however, the patient complained of left flank pain radiating to the left testicle. The following day his temperature rose to 103F. Excretory urograms showed only mild dilatation of the kidney pelves and of the ureters above the site of anastomoses and good function bilaterally. The patient continued to have daily chills and spiking temperature, with a gradual elevation of his nonprotein nitrogen and diminishing of urinary output.

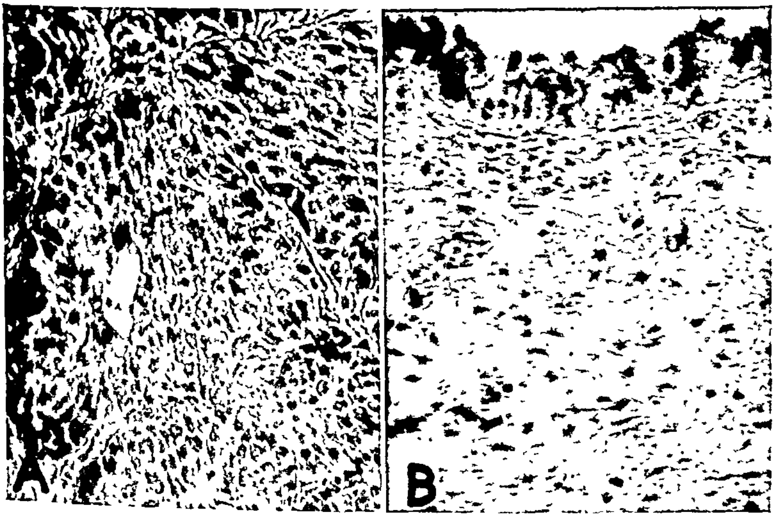

Fig. 1

On September 24 a mass could be palpated in the left lower quadrant and this abscess was drained through a McBurney incision under local anesthesia. This was found to be intraperitoneal and two drains were left in place. Following the incision and drainage, urine began to drain into the wound The urinary output gradually diminished and at the end of 48 hours had completely ceased. The rectal output was also greatly diminished. He continued to run an elevated, septic type of temperature and was given extensive supportive treatment in the form of small blood transfusions, adequate intravenous fluids, and all types of chemotherapy and antibiotics.

The patient's course was progressively downhill and he expired on October 8, 1948.

Postmorten examination was made. The pathologist's report of the urinary bladder is as follows: "The bladder is removed with difficulty because of a moderate amount of perivesical inflammatory reaction. The mucosal surface of the bladder in general is smooth and wrinkled and has a pale pink appearance (fig. 2). There is one area which is slightly firm and elevated measuring 2 mm. in diameter and having a slight hemorrhagic appearance located 1.5 *cm* anteromedially from the right ureteral orifice. Both ureteral orifices are adequate and patent and located in their normal positions. The prostate is small.

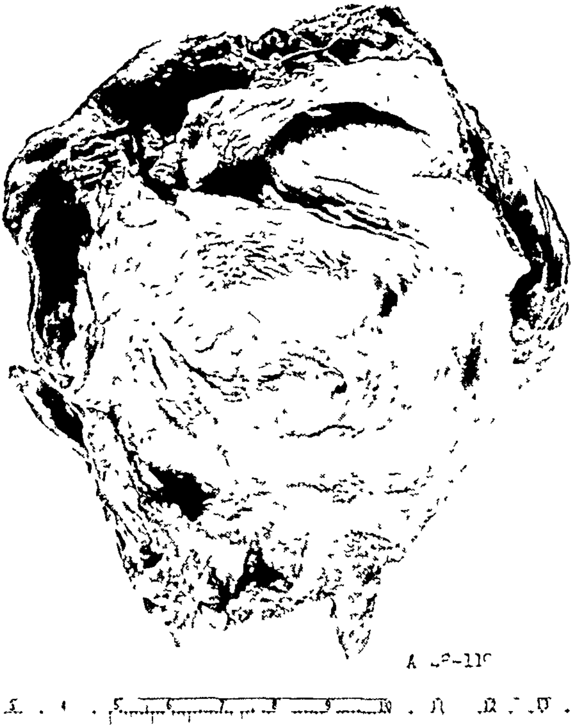

FIG 2

The submucosa in all sections is thickened with edematous vascular and fibrous tissue, variously infiltrated with a few lymphocytes and plasma cells (fig. 1, *B*). In one location, there is a localized hemorrhagic extravasation causing slight disruption of the submucosa which in the same location extends downward into the submucosa to form irregular pits. The cells are three to four layers thick at this point. In another area, there is a similar, but deep extravasation. There is some edema and neutrophilic infiltration in the subserosa. *In no location does one see any carcinoma.*"

SUMMARY

A case report is presented of papillary cancer of the urinary bladder in which the tumor masses regressed subsequent to ureterosigmoidostomy.

No explanation is offered for the disappearance of the tumor following this procedure.

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REFERENCE

GOLDBERG, L. G.: Regression of vesical carcinoma following ureterosigmoidostomy. J. Urol., **63**, 116–121, 1950.

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INFECTED URACHAL CYSTS

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Diseases of the urachus are rarely encountered in daily surgical practice. The authors wish to report 2 cases of infected urachal cysts in infants, in order to stress the diagnostic and therapeutic considerations. Because this disease is infrequently reported in the literature, the report of 2 additional cases is believed to be warranted.

Normally the urachus involutes after being separated from the bladder proper by the development of a mucous fold; all that usually remains is a relatively short strand of a very narrow epithelial tube. This extends upwards in the midline from the anterior wall of the bladder dome to one-third the distance from the bladder to the umbilicus. The tube, though not completedly obliterated, is usually obstructed by cellular debris. If there is failure of normal development, patency of the urachus results. This may be manifest in one of four ways: a) completely patent with openings at the umbilicus and into the bladder; b) communicating with the bladder only; c) communicating with the umbilicus only; d) closed at both ends, but with lumen in between.

Urachal cysts usually exist without clinical evidence. The type which communicates with both the bladder and umbilicus may reveal a fistulous opening draining pus or urine. The internally open and completely blind types may pass undiagnosed, even when the latter is the cause of cyst formation. Urachal cysts, as a rule, become clinically significant if infection occurs. When the cyst becomes purulent, it is termed a pyo-urachus.

The subject of infected urachal cysts was reviewed by Atcheson in 1944, and by Brodie in 1945. Since then a report of internal perforation of an infected urachal cyst with subsequent peritonitis has been given by Blegen in 1946. His patient was treated by closure of the internal perforation with interrupted silk sutures and incision and drainage of the urachal abscess. No further treatment was required, since the urachal lumen became obliterated in the process of healing within a few weeks. Of 2 previously reported cases, quoted by Blegen, 1 patient had general peritonitis, and the other a fistulous communication between the sigmoid and urachal cyst. In his patient, because of abdominal distention and muscular rigidity, only after anesthesia could the urachal mass be felt. In 1944, Atcheson reported 2 cases of patent urachus in soldiers, aged 20 and 21. In one there was urinary drainage, in the other, mucopurulent exudate from the umbilicus. Sibley recently reported a case of infected urachal cyst in a 13-year old boy. Direct trauma to the umbilical region may have been an aggravating factor in development of infection. His patient was treated by marsupialization of the abscess cavity, with excellent result. Dreyfuss states that probably most urachal cysts are retention cysts, although many communicate with the bladder. Some grow to considerable size, as was noted in the case of J. Shelton Horsley, quoted by Dodson, in a 4-year old boy. At operation the cyst was 17 cm. in diameter and weighed 751 gm. However, most of them are small and escape detection for lack of signs or symptoms. More often they become a clinical problem when infection ensues. The cause of the onset of infection is somewhat obscure, but trauma may play a part in its genesis. The situation may be compared to that of pilonidal cysts, where trauma so often is followed by infection. This would be in keeping with the facts that most of the patients are seen after puberty when the chance of appreciable direct trauma is greater. When infection occurs, a tender mass in the hypochondrium may be noted. Rapid increase in size may occur. Gastro-intestinal and bladder symptoms, as well as fever, might be present. Pyo-urachus often drains spontaneously before being recognized. They usually drain through the navel, or into the bladder. The latter will cause pyuria with urinary symptoms. However, the infection may burrow under the abdominal muscles and appear in the groin, or perforate the underlying peritoneum to cause peritonitis. The cause of the peritonitis may not be readily recognized. In those cases in which no external perforation occurred, cystoscopy is valuable. Redness or other inflammatory changes may be noted near the dome of the bladder. Pus may be seen entering from the internal urachal opening. X-ray visualization of the bladder with opaque medium can be very helpful. In cases with drainage into the bladder, direct visualization of the abscess cavity may be possible on cystogram. In unruptured abscess or cyst, the oblique cystogram shows a characteristic concavity of the anterior bladder wall, caused by the overlying urachal mass. By recalling that the urachus lies between the peritoneum and the transversalis fascia and that it develops by tubulation of the upper part of the bladder during descent from the umbilicus into the pelvis, one will realize its proximity to the anterior bladder wall.

BACTERIOLOGY

E. coli, streptococci and staphylococci have been reported as causative organisms. In many cases, the pus was found sterile by smear and culture. This is in keeping with the finding of sterile abscesses in other regions of the body. In one of our cases, hemolytic Staphylococcus aureus was found, while in the other case, the culture was reported sterile.

TREATMENT

As in many surgical cases, antibiotics have wrought considerable change in therapeutic approach. In pyo-urachus, incision and drainage are required. Excision in one stage is hazardous, and the risks are unwarranted. Whereas previously it was believed that excision would be required at a later date, reports have shown that simple drainage, with or without marsupialization, frequently results in destruction of the lining membrane and obliteration of the abscess cavity. However, we believe that in the first of our cases, complete healing was achieved in a relatively short time by laying the cyst open, connecting the numerous pockets, and excising part of the anterior wall. Cultures should be obtained, both of the urine and urachal content. Specific antibiotics and chemotherapeutic management have been found to be useful, both parenterally and by local irrigation. Since rupture into the peritoneal cavity is a real danger, prompt surgical intervention is necessary. Where drainage has spontaneously occurred into the bladder, excision of the urachal sac with closure of the bladder fistula may be required, if obliteration does not occur spontaneously after drainage. In fistulas draining through the umbilicus, vesical neck obstruction may be present, and may require correction before prompt closure of the vesical opening will occur.

CASE REPORTS

Case 1. C. W., Wesson Memorial Hospital No. 69132, a 14-month old male infant, was seen 3 days before admission, because the mother noted protrusion of the umbilicus. A lower abdominal midline mass was palpable, and the child was admitted with the diagnosis of urachal cyst. The infant's behavior pattern had not changed, and except for the mass, there was no reason to believe him ill. On examination, the lower abdomen was prominent. The umbilicus was protruding and everted. A firm, nontender, nonfluctuating mass was palpable in the lower abdomen, extending from 2 cm. above the navel to the symphysis pubis, and laterally to the edges of the recti. On rectal examination, a smooth mass extending deeply into the pelvis was noted.

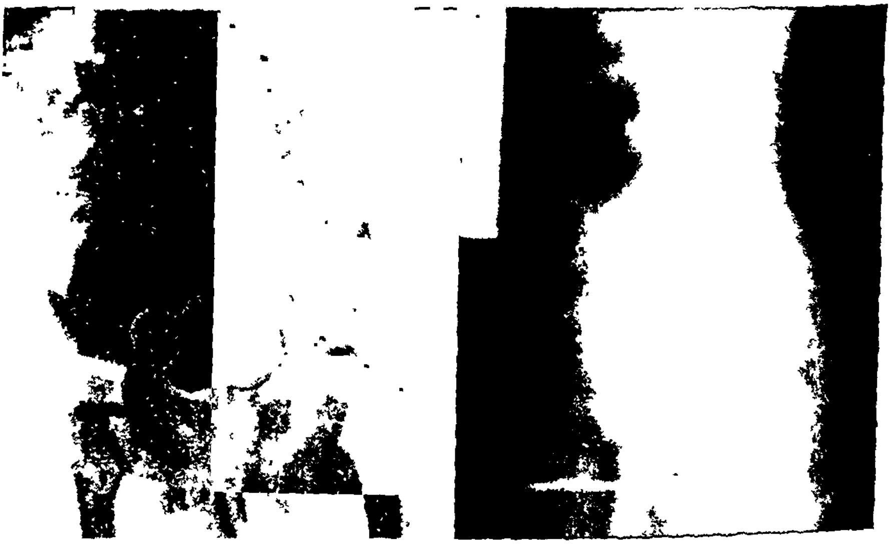

FIG. 1. Case 1. *A*, retrograde cystogram in anteroposterior position demonstrating pressure deformity of bladder dome produced by urachal abscess. *B*, oblique cystogram revealing characteristic concavity of anterior bladder wall caused by the overlying urachal mass

The hemoglobin was 60 per cent, red blood cells 3.70 million; white blood cells 20,900 with 29 per cent lymphocytes, and 65 per cent polymorphonuclears. Two days later, the white blood cell count was 13,500 with 29 per cent lymphocytes and 65 per cent polymorphonuclears.

Catheterization yielded 2 ounces urine, but no change in the size of the mass. Retrograde cystogram revealed a smooth concave pressure defect in the anterior bladder wall on oblique view (fig. 1). Temperature was 100F. There was no change in the local findings and no outward signs of acute inflammation. On the fourth hospital day, incision and drainage of the infected urachal cyst was done. The umbilicus was excised and the loculated abscess was laid open, forming a single cavity. A portion of the anterior wall of the abscess was excised, the cavity packed, and the edges re-united with a few interrupted chromic catgut sutures to prevent gaping.

Smear showed gram positive cocci and culture yielded Staphylococcus aureus. Postoperatively parenteral penicillin and irrigations of the cavity with aqueous penicillin were given. The infant was discharged on the twentieth postoperative day, the abscess cavity becoming progressively smaller and the drainage scantier. During the following 6 weeks, several pieces of catgut extruded through small sinuses. Two months postoperatively there was a solidly-healed, firm scar with no evidence of herniation. Nine month follow-up reveals the infant to be in excellent health.

Case 2. J. O. Jr., Wesson Memorial Hospital No. 42034, age 2½, was admitted March 15, 1941 because of fever and fretfulness of 2 weeks' duration. The child had been fussy for about 2 weeks before admission, and had been vomiting for 3 to 4 days. Physical examination revealed an acutely ill child, temperature 102F, pulse 168. The abdomen was rigid and distended and extremely sensitive to palpation in its lower portion. After 12 days of observation and waiting for localization, an operation was done because of pre- and postoperative diagnosis of appendicitis with perforation and peri-appendiceal abscess. A lower right rectus incision was made and fascia and peritoneum ruptured spontaneously after handling with blunt end of scalpel. About 300 cc of foul smelling, greenish-yellow pus was released. Two Penrose drains were placed for drainage, and the abdominal wall closed. Child was discharged on the nineteenth postoperative day with operative wound still draining. Culture of the fluid was sterile. The urinalysis was negative. Blood count: 3.3–4.3 million red blood cells, hemoglobin 55–82 per cent, white blood cells 24,800 with 90 per cent polymorphonuclears. He was readmitted 2 weeks after discharge because the mother noted purulent discharge from the umbilicus. Examination of the abdomen revealed small amount of purulent drainage, both from the umbilicus and the incision in the right lower quadrant. The hemoglobin was 62 per cent, white blood cells 10,700 with 54 per cent polymorphonuclears. The sinus tract was injected with contrast medium, demonstrating tract to run downward toward the cecum and then upward to the umbilicus (fig. 1). The temperature course was normal. The sinus tract was irrigated with Dakin's solution, ST 37, and saturated solution of urea. Five weeks later the child was discharged to the out-patient department for continued irrigations. The discharge diagnosis was "sinus after drainage of peri-appendiceal abscess."

One year later, the child was readmitted with persistent drainage from the wound. Other than constipation, the child was progressing satisfactorily. Examination revealed a firm scar in the right lower quadrant that contained a draining sinus. The operative note reads as follows: "The ileum and cecum were adherent to the scar. The appendix was swollen and in close proximity to the sinus tract.

The lumen of the tract was filled with thick creamy pus. Considerable inflammatory adhesions were present throughout. The thickened sinus tract extended to the dome of the bladder and was firmly adherent. The ileum and cecum were freed and the appendix removed. The sinus tract was freed and dissected from the bladder wall. Grossly no lumenal connection was noted with the bladder. the bladder was reperitonealized, and the wound closed with silkworm sutures and clips." The pathological report was urachal remnant and chronic appendicitis. The urine contained 1 plus albumin and many bacteria. Blood count was within normal limits. The postoperative course was rather uneventful, and the child was discharged on the eighteenth postoperative day. The wound healed by primary intention.

SUMMARY

Two cases of infected urachal cyst in infancy are presented. One cyst in a 14-month old boy was diagnosed preoperatively and treated by a modified form of marsupialization. In the second case, involving a 2½ year old boy, an appendiceal abscess was; simulated, and after drainage, resection of the cyst wall was necessary. Reviewing the recent literature we find support in our belief that cure can be obtained with the help of antibiotics and adequate drainage of the cyst. This should make the need for secondary operations less frequent.

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REFERENCES

Atcheson, D. W.: J. Urol., **51:** 424–430, 1944.
Blegen, H. M.: Northwest. Med., **45:** 838–839, 1946.
Brodie, N.: Am. Surg., **69:** 243–248, 1945.
Dodson, A. I.: Urological Surgery. St. Louis: C. V. Mosby Co., 1944.
Dreyfuss, M. L.: Virginia Med. Monthly, **70:** 200–204, 1943.
Sibley, W. L.: Am. J. Surg., **79:** 465–468, 1950.

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PRIAPISM IN SICKLE CELL ANEMIA*

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Our paper will be limited to priapism occurring in sickle cell anemia, which constitutes a subgroup of diseases and injuries of the vascular and hematopoietic systems. Priapism associated with sickle cell anemia has been recorded previously in 16 instances.†

During a 10 year period (1940–1950) there were 159,690 admissions to the Shreveport Charity Hospital and approximately two-thirds of the admissions were Negroes. Sickle cell anemia was found in 181 instances (102 males and 79 females) of these Negro admissions. Priapism was the chief complaint in 5 cases.

REPORT OF CASES

Case 1. N. D. (No. 415928), a 5 year old Negro boy, was admitted to Shreveport Charity Hospital September 8, 1941 with the chief complaint of persistent and painful erection of the penis and difficulty in urinating of 4 days' duration. Eight days prior to admission, he developed fever, abdominal pains, jaundice and "rheumatic pains" in his joints. The past history revealed the presence of repeated attacks of fever, jaundice and "rheumatic pains" in his joints. Also the family history revealed that his father, paternal aunt and an older sister had similar symptoms of fever and jaundice.

The patient appeared to be in pain and acutely ill. The temperature was 103.2F. The scleras were icteric and the penis was completely erected and painful on manipulation. There was tenderness in the suprapubic region as the bladder was distended.

Laboratory examination revealed 5 gm. hemoglobin, 1,670,000 red blood cells, 53,000 white blood cells and a differential count of 82 polymorphonuclear neutrophils, 4 stabs 2 polymorphonuclear eosinophils, 7 lymphocytes, 2 large mononuclears, 1 juvenile and 2 nucleated red blood cells. There was 40 per cent sickling of the red blood cells as well as moderate poikilocytosis, achromia, polychromatophilia and macrocytosis. The icteric index was 21.5 units and the fragility test revealed hemolysis beginning at 0.36 per cent NaCl and ending at 0.22 per cent NaCl.

Therapy consisted of catheterization, choral hydrate, tincture of belladonna, codeine sulfate, sodium bromide, ice packs to the penis and three blood transfusions of 300 cc each. During his hospital course, his temperature curve was septic, varying from 103.2 to 104.4F for 5 days. Ten days after the onset of the priapism he received his second transfusion. At this time the fever subsided and the priapism began to disappear. As his condition improved, the laboratory findings also showed improvement. The icteric index fell to 16.0 units and the total white count fell to 20,100. He was discharged October 7, 1941 with slight evidence of priapism. The blood picture revealed 12,000 white blood cells with 57 polymorphonuclear neutrophils, 7 polymorphonuclear eosinophils, 3 stabs and 33 lymphocytes. The red blood cell count was 3,950,000 and the hemoglobin was 10.5 gm.

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* In this paper sickle cell anemia refers to sickle cell disease with and without anemia.

† Oberndorf (1934), Diggs and Ching (1934), Campbell, 2 cases (1935), Dawson, 2 cases (1939), Getzoff, 3 cases (1942), Phillips (1944), Rosokoff and Brodie (1946), Grover (1947), Harrison (1947), Sawan and Cawley (1947), Levant and Stept (1948), Kemp and Hosay (1950).

A follow-up of 8½ years revealed that (age of 14) the patient showed the typical features of sickle cell anemia. He weighed 88 pounds and was 64.5 inches in height. He had had 5 blood transfusions since discharge. So far as could be determined, there was no evidency of impotency.

Case 2. S. J. (No. 425278), a 19 year old Negro, was admitted to Shreveport Charity Hospital on April 20, 1942 with the history of having been awakened by a persistent painful erection of the penis on the morning of April 12, 1942. He had a previous attack 47 days before admission which was not relieved by sexual intercourse of 4 hours' duration, but the priapism disappeared of its own accord 5 hours later. A second attack occurred March 14, 1942 and disappeared within approximately 24 hours without specific treatment. The present attack had been persistent, painful and of 8 days' duration. He gave no history of difficult urination or traumatic injury. The past history revealed repeated attacks of "rheumatic pains" and "arthritis" of his knees, shoulders, and elbows since early childhood. He had gonorrhea 1½ months prior to admission which was treated by urethral injections and a liquid medicine by mouth.

The patient did not appear to be in severe pain. His temperature was 100.6F; the pulse was 100/minute and the blood pressure was 120/76. The scleras were slightly icteric and the inguinal lymph nodes were palpable. The penis was erect and tender to manipulation. There was no urethral discharge. The prostate gland was tender and slightly enlarged.

Laboratory examination disclosed a trace of albumin in the urine and the serology was negative. The white blood cell count was 11,650 with 54 polymorphonuclear neutrophils, 31 lymphocytes, 5 large mononuclears and 10 stabs. The red blood cell count was 4,320,000 and the hemoglobin was 14 gm. There was slight poikilocytosis, anisocytosis and an occasional target cell. The sickle cell preparation showed 95 per cent sickling.

Therapy consisted of codeine sulfate, morphine sulfate, sodium bromide and hot compresses to the penis. The temperature curve varied from 100 to 101F daily. The priapism began to subside on the third day of hospitalization and the patient signed a release from the hospital. The attempt at clinical follow-up was not successful.

Case 3. A. J. (No. 434746), a 33 year old Negro, entered Shreveport Charity Hospital December 26, 1942 with the complaint of persistent penile erection of 3 weeks' duration. His first attack of priapism began 9 months prior to hospitalization, at which time it lasted only 2 to 3 hours. Three months prior to his admission to the hospital an attack occurred and the penis remained in a partially erected state. Three weeks prior to admission the penis became completely erected and the condition persisted. In addition, he had had a "low grade fever." The past history disclosed that he had had numerous attacks of vague abdominal pain which were accompanied by fever and jaundice. Also the patient had gonorrhea in 1932 and pneumonia in 1928.

The patient did not appear acutely ill. The temperature was 100.6F, the pulse 104 and the blood pressure was 116/80. The penis was completely erected and the corpora cavernosa were tense and tender to palpation. Apparently the corpus spongiosum and glans penis were not involved. The prostate gland was slightly enlarged, soft and tender.

The laboratory examination revealed 3,950,000 red blood cells, 10.5 gm. hemoglobin, 11,100 white blood cells with 60 polymorphonuclear neutrophils, 5 stabs, 32 lymphocytes and 3 monocytes. There were many target cells as well as slight poikilocytosis, anisocytosis, moderate hypochromia and polychromatophilia. There was 95 per cent sickling of the red blood cells. The serology was negative and the urinalysis was essentially negative. A chest x-ray and a plain urogram were without significant findings.

In regard to the hospital course, the patient had a temperature of 102F for 4 days.

Treatment consisted of hot sitz baths, stilbestrol, sedation and a saddle block of 100 mg. novocain. On the sixth day of hospitalization, there was evidence of improvement of the priapism, and the patient was discharged January 11, 1943.

Case 4. J. R. W. (No. 476656), a 28 year old Negro, was admitted to Shreveport Charity Hospital May 18, 1946 with the chief complaint of persistent penile erection of 2 weeks' duration. His first attack of priapism began 4 months before admission to the hospital and the attack subsided within 4 hours without treatment. Approximately 2 months prior to hospitalization he developed priapism again which partially subsided and for the past 2 weeks the penis had been completely erect and accompanied by pain. The patient stated that he had had fever for the past 7 days. His past history revealed that there had been repeated attacks of vague abdominal pain and fever since childhood. In addition, he had gonorrhea 1 year prior to admission.

The patient did not appear acutely ill. The temperature was 100F, the blood pressure 120/86 and the pulse was 110 per minute. The penis was completely erect and tender to palpation. The corpora cavernosa were tense and tender. The prostate gland was soft, smooth, nontender and not enlarged. A chest film and a plain urogram were reported as negative.

The nonprotein nitrogen was 26 mg. per 100 cc; red blood cell count 3,200,000; hemoglobin 9.5 gm.; white blood cell count 12,000 and moderate poikilocytosis, achromia and polychromatophilia. The sickle cell preparation revealed 85 per cent sickling. The spinal fluid showed no remarkable changes.

In the hospital the patient continued to have slight fever.

Therapy consisted of caudal block, spinal anesthesia consisting of 100 mg. of monocain, sedation and stilbestrol.

The priapism showed partial regression, but the penis remained in a semi-erectile state at the time of discharge on June 10, 1946. A 4 year follow-up revealed that the patient had had mild attacks of priapism but none that had required hospitalization. The patient denied being impotent.

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The priapism showed partial regression, but the penis remained in a semierectile state at the time of discharge on June 10, 1946. A 4 year follow-up revealed that the patient had had mild attacks of priapism but none that had required hospitalization. The patient denied being impotent.

Case 5. W. C. (No. 514899), a 9 year old Negro boy, entered Shreveport Charity Hospital September 3, 1948 with the complaint of painful persistent erection of the penis and abdominal pain of 2 days' duration. The erect penis had gradually become painful since the onset of the attack. The past history revealed frequent episodes of vague pains in his legs, arms, and abdomen. There was no family history of anemia. The patient was undernourished and poorly developed. The temperature was 100F and the blood pressure was 128/78. The penis was completely erect and painful on manipulation. The cervical lymph nodes were enlarged.

Laboratory examination showed a negative serology; 3,370,000 red blood cells; 24,500 white blood cells, with 72 polymorphonuclear neutrophils, 3 stabs, 9 lymphocytes, 14 monocytes and 2 polymorphonuclear eosinophils. There was a moderate poikilocytosis, hypochromia, slight anisocytosis, and polychromatophilia. An occasional target cell was present. There was 98 per cent sickling of the red cells. The icteric index was 17 units. An excretory urogram, x-ray of the chest, serology, urinalysis and blood chemistry were not significant.

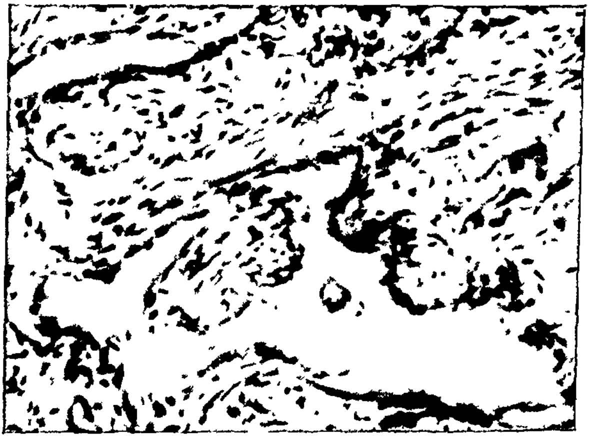

FIG 1 Note well-formed patent cavernous spaces

Therapy consisted of 1 mg. stilbestrol 3 times a day. Three to four cubic centimeters of thick dark grumous blood was aspirated from the crura and corpora cavernosa, and the corpora cavernosa were irrigated with normal saline. In addition, hot packs were applied to the penis.

Following the aspiration and irrigation of the corpora cavernosa, the priapism partially subsided. When the patient was discharged on September 15, 1948 the priapism had subsided completely.

The patient was readmitted to the hospital May 12, 1950 for further studies. He had been impotent since the last admission. Laboratory examination showed 3,500,000 red blood cells with 10 gm. hemoglobin and 100 per cent sickling. Icteric index was 20.4 units. The patient was given two transfusions of 300 cc of blood. Under spinal anesthesia a circumcision was performed and at the same time a biopsy of the corpora cavernosa was taken.

Sections of the corpus cavernosum revealed well-formed patent cavernous spaces. The trabeculae showed slight evidence of interstitial edema and fibrosis. In addition, there was infiltration of an occasional lymphocyte and monocyte. Whether or not these findings produced narrowing of the cavernous spaces was difficult to determine from the sections. A few sickled red blood cells were present in the small blood vessels (fig. 1).

The patient was discharged on May 20, 1950 after an uneventful postoperative course.

DISCUSSION

Persistent erection of the penis and pain on manipulation of the penis are the chief symptoms. Previous episodes of penile erection of short duration and without sexual desire may have occurred. Usually, symptoms of sickle cell anemia are present. These symptoms consist of fever, jaundice, anemia, vague pains in the abdomen and joints, weakness and leg ulcers. The family history may reveal the presence of symptoms associated with sickle cell anemia. Urinary symptoms are uncommon; however, one of our cases (N.D.) complained of the inability to urinate. No history of previous injury or trauma was obtained in our cases.

Priapism associated with sickle cell anemia has been previously recorded in patients from 8 to 29 years of age. In our series of cases it was found to occur in patients from 5 to 33 years of age. It is not found after 40 years of age, since patients with sickle cell anemia rarely live beyond that age.

In the prone position, the penis is usually maintained at an acute angle to the pubis. On palpation, the corpus spongiosum is soft and apparently not involved. The corpora cavernosa are uniformly hard and painful. The typical sickle cell anemia facies consisting of generalized hypoplasia, spindle legs, bluish-green scleras, asthenic status and leg ulcers may or may not be present.

The diagnosis of sickle cell anemia depends upon the laboratory demonstration of the sickled red blood cells and the associated anemia. Priapism due to other etiological causes must be ruled out in patients with sickle cell anemia. A review of the autopsy records of 16 cases of sickle cell anemia revealed the following associated diseases or conditions: Carcinoma of the kidney, typhoid fever, tularemia, hypertensive cardiovascular disease, nonsuppurative encephalitis, peritonitis, tuberculosis, syphilis, bronchopneumonia, lung abscess and acute yellow atrophy of the liver.

The exact mechanism of the thrombosis or pseudothrombosis of the vascular system of the penis occurring in sickle cell anemia is obscure. Diggs and Ching proposed that the congestion and capillary engorgement of the tissues were due to the interlocking and the resistance encountered in passage of the spiked and elongated red blood cells in the capillaries. Murphy and Shapiro observed that there was a progressive rise in the number of sickle cells in the circulating blood preceding a crisis and as a susceptible erythrocyte became older, sickling was more pronounced. Hahn and Gillespie explained that a susceptible erythrocyte would sickle only if its hemoglobin was in a reduced state. In addition, these authors discovered that an oxygen tension of 45 mm. of mercury was necessary to produce sickling. Krogh and also Landis reported that capillary anoxia damaged the lining cells and rendered them more permeable to plasma and as plasma escaped, hemoconcentration resulted which tended to stagnate the blood and build up the carbon dioxide content. These changes in turn tended to produce sickling of the susceptible erythrocytes. If these observations are facts, priapism in sickle cell anemia could be precipitated by constriction of the venous blood supply of the penis in susceptible patients.

A review of the literature fails to reveal any previous study of the histopathology of the corpora cavernosa in sickle cell anemia. No definite conclusion can be made from the case that we have studied. The sections showed no specific findings. However, from the sections it can be definitely stated that there were no organized thrombi in the cavernous spaces.

Caudal anesthesia, hypnosis, spinal anesthesia, sedation, intravenous mercurochrome, oxygen inhalation, x-ray, estrogens, transfusions, aspiration of the corpora, multiple surgical incisions of the corpora, hot and cold compresses have been employed in the treatment of priapism occurring in sickle cell anemia.

We believe that small multiple transfusions is the treatment of choice. It is important to use blood that does not show the sickling trait in order to increase the erythrocyte count of the blood stream and to insure an average 120 days life span of the cell rather than the 20 days life span of the sickle cell. Sedation is used as needed.

Certainly there is no indication for radical surgery in the treatment of priapism occurring in sickle cell anemia, since all of the previously recorded cases, as well as our 5 cases, did not develop gangrene.

Six of the previously recorded cases* were described as being impotent. In the remaining cases no reference was made on this subject. It is judged that the cases were not followed long enough to determine potency. All six of these cases had been treated either by aspiration of the corpora cavernosa or by multiple surgical incisions. The only case we treated by aspiration of the corpora cavernosa also became impotent. Therefore, there appears to be a direct relationship between aspiration or incision of the corpora cavernosa and the development of impotency.

SUMMARY

Five cases of priapism complicating sickle cell anemia and occurring in Negroes whose ages varied from 5 to 33 years are presented and the previously reported cases are briefly reviewed. Clinical follow-up consisting of 1½, 4 and 8 years, respectively, is available in 3 cases. A short discussion of the symptoms, physical findings, diagnosis, physiopathology and treatment is given.

CONCLUSIONS

Priapism may be the chief complaint of Negro males with sickle cell anemia.

Impotency is prone to occur in the patients who are treated by aspiration or incision drainage of the corpora cavernosa.

Histopathologic study of the corpora cavernosa in one of our patients who had recovered from priapism revealed no evidence of thrombosis of the cavernous spaces.

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* Hahn, Harrison, Kemp, Levant and Stept, Phillips, Rosokoff and Brodie.

REFERENCES

Bailey, H.: Brit. J. Surg., **35:** 298–303, 1948.
Campbell, E. H. Jr.: Arch. Surg., **31:** 607–621, 1935.
Cave, W. H.: Am. J. Surg., **61:** 305–307, 1943.
Dawson, G. R., Jr.: J. Urol. **42:** 821–829, 1939.
Diggs, L. W. and Ching, R. E.: S. Med. J. **27:** 839–845, 1934.
Getzoff, P. L.: J. Urol., **48:** 407–411, 1942.
Getzoff, P. L.: Personal communication.
Grover, V.: Ann. Int. Med. **26:** 843–851, 1947.
Hahn, E. V. and Gillespie, E. B.: Arch. Int. Med. **39:** 233–254, 1927.
Hahn, E. V. and Gillespie, E. B.: Am. J. M. Sc. **175:** 206–217, 1928.
Harrison, F. G.: Penn. Med. J., **50:** 1074–1078, 1947.
Hinman, F.: Ann. Surg., **60:** 689–716, 1914.
Kemp, N. F. and Hosay, J. J.: Urol. Cutan. Rev., **54:** 69–72, 1950.
Krogh, A.: Anatomy and Physiology of the Capillaries. New Haven: Yale University Press, 1929, 2nd ed.
Landis, E. M.: Am. J. Med. Sc., **193:** 297–313, 1937.
Levant, B. and Stept, R.: J. Urol., **59:** 328–329, 1948.
Murphy, R. C. Jr. and Shapiro, S.: Arch. Int. Med., **74:** 28–35, 1944.
Oberndorf, C. P.: Arch. Neurol. & Psychiat., **31:** 1292–1296, 1934.
Phillips, A. A.: J. Nat. Med. Assn. **36:** 88–90, 1944.
Rosokoff, J. and Brodie, E. L.· J. Urol., **56:** 544–546, 1946.
Sawan, E. and Cawley, R. D.: Clin. Pro. of Child Hosp., **3:** 241–243, 1947.

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PENILE HORN

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Cutaneous horns are a peculiar form of cutaneous wart characterized by an excessive and increasing keratosis.[1] These are most common on the scalp but have been reported to occur in many locations.

Seven cases of penile horn previously have been reported in North American literature. The first case was reported by Jewett in 1854.[2] Since that time cases have been reported by Brinton,[3] Young,[4] Van Der Velde,[5] Goldstein,[6] Taylor,[7] and O'Crowley.[8] The cases reported by Young and by Goldstein were unique in that 2 horns occurred on the penis in the same patient simultaneously.

Van Der Velde in a review of the literature was able to find 24 cases reported in the European writings.[5]

CASE REPORT

L. A., a 53 year old white farmer, was admitted to the Indianapolis Veterans Hospital December 21, 1949. The chief complaint was a painful, horny growth on the penis. Fifteen months prior to admission the patient complained of pain about the glans penis and the inability to retract the prepuce. Circumcision was advised and performed, but the soreness of the glans persisted and a warty growth soon appeared. The wart grew rapidly and in a short time a horn appeared which gradually increased in size during the year before admission. On several occasions the patient trimmed the horn with his pocket knife to reduce its size. He consulted his physician because of the malady and local applications to control the pain were prescribed. But tenderness and pain at the base of the lesion were practically constant and finally brought the patient to us.

The positive findings on examination were: blood pressure, 178/102; an irregularity of the pupils; and a horny growth on the penis. The penile horn was located on the left side of the glans at the junction with the shaft. The base of the lesion was 4 cm. in diameter and the length of the horn was 7 cm. The base was tender and reddened with a tendency toward piling up of the edges; it was laminated and grayish yellow in color (fig. 1, *A*). The inguinal nodes were enlarged bilaterally.

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Read at annual meeting, North Central Section, American Urological Association, Milwaukee, Wis. October 13, 1950.

[1] Ewing, J. E.: Neoplastic Diseases. Philadelphia: W. B. Saunders Co., 1940.

[2] Jewett: New York Med. Times, 1854.

[3] Brinton: J. Cutan. & G. U. Dis., July 1887.

[4] Young, H. H. and Davis, D. M.: Young's Practice of Urology. Philadelphia: W. B. Saunders Co., 1926.

[5] Van Der Velde, O.: J. Mich. St. Med. Soc., **35:** 317, 1936.

[6] Goldstein, H. H.: J. Urol., **30:** 367, 1933.

[7] Taylor, J. A.: Trans. American Assoc. Genito-Urin Surg.; **37:** 101, 1944.

[8] O'Crowley, C. R.: Discussion. Trans. Am. Assoc. of Genito-Urin Surg., **37:** 107, 1944.

The serologic examination for syphilis was negative. X-ray of the chest was within normal limits.

The clinical diagnosis was "probable carcinoma of the penis with epithelial horn formation."

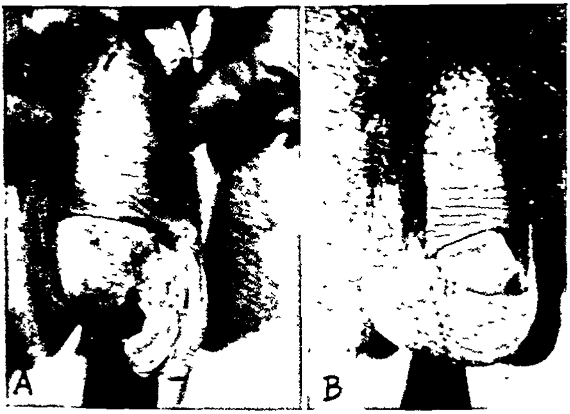

FIG. 1

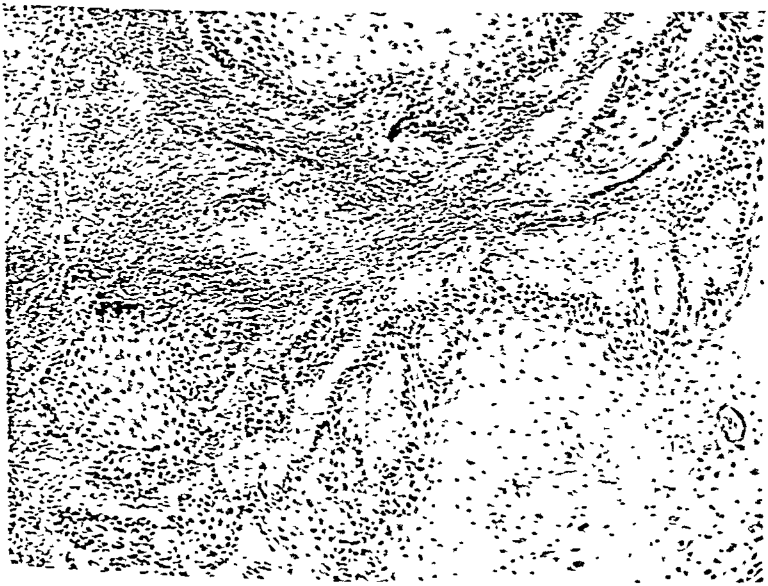

FIG 2

The lesion was excised with electrosurgical technique on December 30, 1949, along with removal of an inguinal lymph node for biopsy. The base of the growth was removed with a margin of 2–3 mm. of normal skin and, in order to adequately remove the lesion, a thin layer of the corpus spongiosum was removed. The edges of the latter were approximated with interrupted sutures of fine chromic catgut, but the remainder of the wound, which was quite large, was left to granulate because it was felt that closure would result in too much constriction. A No. 18 Foley catheter was anchored in place at the end of the procedure to facilitate cleanliness of the wound and dressings.

The postoperative course was uncomplicated. Penicillin was given prophylactically. The wound was kept clean by the use of wet saline dressings when the slough began to separate. Epithelialization was complete in eight weeks, and examination at that time revealed only a mild degree of chordee. The patient was last seen on June 20, 1950 (fig. 1, *B*) when he reported normal urination and no interference with sexual intercourse.

Pathological report (Dr. David Rosenbaum): "Sections through the base of the lesion show a very great proliferation of stratified squamous epithelium downward into the underlying connective tissue. The epithelial cells grow in sheets, strands and nests and most of them are limited by a basement membrane. However, in some places, the basement membranes have lost their integrity and cells of epithelial origin are seen in the stroma. Some of the cells are atypical in appearance but most of them tend to be of mature stratified squamous type. Mitotic figures are rare" (fig. 2). The hardened portions of the lesion showed enormously thickened parakeratotic epithelium. The diagnosis was squamous cell carcinoma, grade 1, of the penis with epithelial horn formation.

The microscopic examination of the lymph nodes showed a slight reactive hyperplasia.

DISCUSSION

Cutaneous horns usually begin as a wart on normal skin or in scars. Warts and papillomatous growths on the penis occur most frequently in those patients with redundant prepuces who seldom retract the foreskin for reasons of cleanliness. We believe that irritation of the glans, as was true in our case, is the most important etiologic agent in the development of warts, carcinoma and subsequently in a few cases cutaneous horns. Why do not all patients with warts and carcinoma of the penis develop cutaneous horns? This question is as yet unanswered. Perhaps a virus infection, such as was incriminated in cottontailed rabbits as causing horny growths, could be the answer.[9]

Cutaneous horns are lesions characterized by keratosis or a pathologic epidermoid proliferation. Keratosis has long been known to be a precursor of carcinoma, and in our case the picture of carcinomatous change was definitely present. Lebert found that 12 per cent of the cases of cutaneous horn he reported developed carcinoma.[10] The cases reported by Van Der Velde, Goldstein, and Taylor all were reported as carcinoma with horn formation. In all cases demonstrating epithelial horn formation on the penis carcinoma must be ruled out.

We believe that the treatment of choice is excision with electrosurgical technique. With this method the operation is easily performed in the minimum of time with little blood loss. In removal of the lesion a margin of normal tissue about the base must be removed to prevent recurrence. Young[4] pointed out that

[9] Huggins, C. B.: Ibid.

[10] Lebert: Keratose, Breaslau, 1864.

removal of the horn without excising the skin and underlying growth resulted in failure of treatment. In lesions that are unusually large amputation of the penis must be considered, and as a matter of fact, this possibility was discussed with the patient. Van Der Velde[5] was of the opinion that amputation of the penis was the one and only successful method of treatment. The smooth and rapid healing in this case, the prompt disappearance of the inguinal adenopathy, and the subsequent course, even though the interval is much too short, leads us to agree with Young that wide local excision will suffice when feasible.

SUMMARY

A case of cutaneous horn of the penis has been reported which was treated successfully by electrosurgical excision.

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INTERSTITIAL CELL TUMOR OF TESTIS

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Recently Melicow, et al., reported the tenth case of interstitial cell tumor of the testis occurring in childhood. These authors presented an excellent discussion of the subject of Leydig cell tumors and a review of the literature. Reiners and Horn subsequently reported 2 cases in adults, bringing the total number of published cases in adults to 29. The purpose of this paper is to present the thirtieth case in adults, the first to have a simple enucleation of the neoplasm.

CASE REPORT

J. K. D., Hospital No. 84428, a 32 year old white man, Coast Guard, was admitted to the U. S. Marine Hospital, Baltimore, on August 21, 1948, complaining of fatigue, pain and swelling of both ankles, gynecomastia, and progressive loss of libido.

He gave a history of having been kicked in the genitalia during early youth resulting in atrophy of the right testicle. In 1944 the patient first noted bilateral gynecomastia which was progressive to the time of admission. For 2 years prior to admission the patient complained of increasing loss of libido. He was still able, however, at the time of admission, to have intercourse.

In 1946 the patient suffered a "stroke" resulting in paralysis of the left half of his body. This cleared except for minimal residual sensory changes. Soon after this episode he began to experience transient but rather severe substernal pain which recurred frequently during the 2 years preceding admission. The attacks of substernal pain were precipitated usually by rapid walking or heavy work.

Two months prior to admission he first complained of vague pains in the lower legs and calves with swelling and tenderness in both Achilles' tendons.

Physical examination on admission showed pronounced bilateral gynecomastia (fig. 1). The patient walked with a limp favoring the left leg. Each Achilles' tendon was thickened 3 to 5 times normal size and was tender on palpation. A nodule measuring 0.5 cm in diameter was palpable in the Achilles' tendon of the left gastrocnemius muscle. Both tendons felt hard in the midportions. This was more marked in the left tendon.

Examination of the external genitalia revealed the right testicle to be approximately $\frac{1}{3}$ normal size. The left testicle was slightly smaller than normal. The epididymis on the left was normal. In the upper portion of the left testicle adjacent to the head of the epididymis was a definite, well isolated, almost stony hard nodule which was felt to be within the parenchyma. Cord structures were normal. Rectal examination revealed no evidence of prostatic enlargement and the seminal vesicles were not palpable.

Other physical findings were within normal limits.

Laboratory data: White blood count, red blood count, urinalysis, and serological tests for syphilis were normal. Total cholesterol varied from 474 mg. per cent to 559 mg. per cent (normal 180 mg. per cent to 220 mg. per cent). Tests of liver function, including zinc sulphate, thymol turbidity, cephal in flocculation, icterus index, and serum bilirubin were within normal limits. Uric acid 2.9 mg. per cent, calcium 10.1 mg. per cent, inorganic phosphorus 2.5 mg. per cent, serum amylase 111 units. Repeated basal metabolic tests were normal or slightly depressed. X-rays of both Achilles' tendons, the long bones, skull, and chest were normal. An excretory urogram revealed no abnormalities. Friedman reaction was negative.

The patient was admitted to the orthopedic service because of the acute symptoms referable to the Achilles' tendons. Biopsy of the tendon masses revealed typical xanthomatous changes. He was treated with low cholesterol diet during his hospital stay.

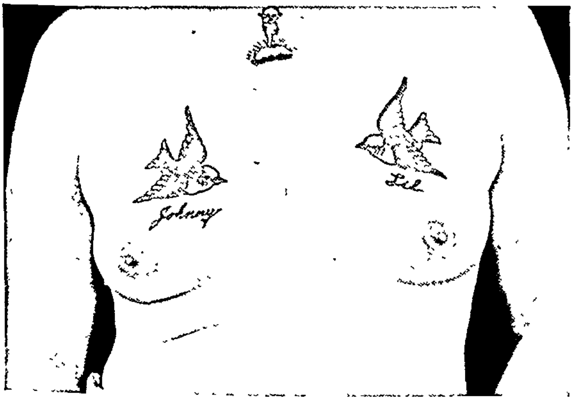

Fig. 1. Patient

He was seen in consultation by the urology service because of the gynecomastia, loss of libido, and the left testicular mass. Because of the atrophic right testicle and progressive loss of libido, the patient refused to have the left testicle removed. Before submitting to surgery, therefore, the patient had to be assured that only the tumor nodule and not the testicle was to be excised. It was explained that a frozen section would be obtained at the time of surgery and only if carcinoma were found would the testicle be removed. Under these circumstances an exploratory operation was performed on October 21, 1948.

A well isolated nodule which measured 1 cm. in diameter was found embedded in the parenchyma in the upper portion of the left testicle. The nodule was firm, well encapsulated, and was enucleated with ease. Frozen sections were made and because no definite diagnosis was offered, the wound was closed. The postoperative course was uneventful.

Pathological report (C. H. Binford, M.D.): The specimen was a firm, rounded mass slightly over 1 cm in diameter. On section the color was brown.

Microscopic: A thin fibrous capsule irregularly separated the tumor from testis and epididymis. Branching from this capsule collagenous trabeculae divided the tumor into variously sized lobules. The tumor pattern consisted of a very delicate vascular stroma which supported clusters of closely coherent polyhedral cells of 16 to 20 μ in diameter. Nuclei were uniformly medium sized and vesicular. Nucleoli were prominent. Cytoplasmic zones were granular, finely vacuolated, or clear. The overall pattern of the tumor was somewhat suggestive of adrenal cortex. Cells undergoing mitotic change were not observed. Small masses of tumor cells were found outside of the capsule and while an occasional extracapsular mass suggested that it might be in a lymphatic space, definite lymphatic invasion was not demonstrated. Within some of the tumor cells were rod-shaped bodies about 1 by 1 by 10 μ which were stained pink by Romanowsky stain. These bodies appeared to be morphologically consistent with so-called "crystalloids" (fig. 2).

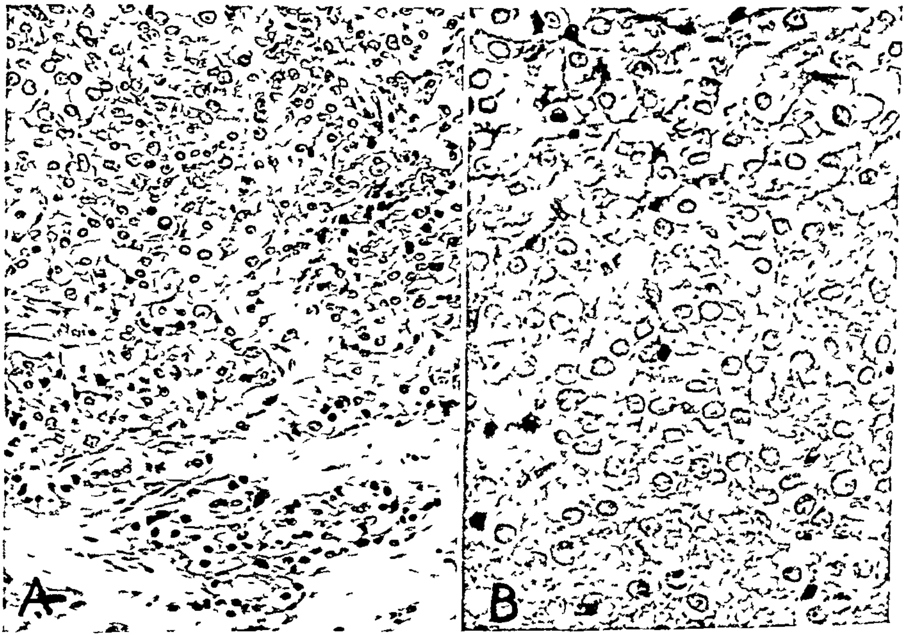

FIG 2 *A*, photomicrograph of tumor × 150, *B*, photomicrograph of tumor × 300

A Sudan IV stain of a frozen section revealed an appreciable number of orange stained fine globules within tumor cells. On the polarized light this lipoid was isotropic.

The tumor was seen by several other pathologists including Dr. Harold Stewart of the National Cancer Institute, Bethesda, Maryland; Dr. Fred Stewart, Memorial Hospital, New York City; and Dr. S. K. Mostofi of the Armed Forces Institute of Pathology. All agreed that the diagnosis was "interstitial cell tumor of the testis."

Dr. Mostofi discussed the possibility of a diagnosis of androblastoma, but stated that the presence of the crystalline inclusions should place the tumor in the interstitial cell group.

The patient refused further surgery. He was asymptomatic at the time of discharge although there had been no breast changes.

Although the patient was advised to do so he did not return to this hospital for treatment.

He was subsequently admitted to the U. S. Naval Hospital, Philadelphia, on September 12, 1949. The following clinical course summary was received from the U. S. Naval Hospital:

On the day of admission the patient noted a sudden onset of severe substernal pain and perspiration. A local physician was called who administered morphine and referred the patient to the hospital with a tentative diagnosis of myocardial infarction. At the time of admission the patient complained of substernal pain which had not been relieved by the medication given previously. He was restless, in some respiratory distress, and coughing frequently. Physical examination of the heart revealed no abnormalities. Blood pressure 94/64. He was given oxygen, aminophyllin, and sodium amytal. In spite of supportive measures he suddenly became comatose and intensely cyanotic. Tourniquets were applied to the extremities but the patient died 25 minutes after admission to the hospital.

Permission for autopsy was granted. Findings were as follows: 1) coronary occlusive disease with myocardial infarction; 2) pulmonary edema; 3) chronic passive congestion of liver; 4) deformity of right wrist.

Inquiry concerning the genitalia and breasts revealed that the pathologist had noted no gynecomastia. Microscopic examination of the breasts was not carried out. Both testes were normal grossly and microscopically.

DISCUSSION

An interesting observation in this case has been the associated coronary artery disease, xanthoma formation and hypercholesterolemia. Elevated cholesterol levels may have been either a result of the xanthoma or possibly of the coronary artery disease. Mathé has reported a case of interstitial cell testicular tumor associated with a xanthoma of the abdominal wall. It may be of significance that of the 30 interstitial cell tumors described in adults, 2 should have associated xanthomas. Unfortunately, cholesterol levels were not reported in Mathé's case.

Interstitial cell tumors in mice have been experimentally produced following administration of stilbestrol. Interstitial cell hyperplasia in man has been described following vasectomy, partial castration, cryptorchism, transplantation of testicles, in tuberculosis, syphilis, carcinoma, atrophy of testes with hypothyroidism, cirrhosis, chronic alcoholism, and after administration of estrogens. It is again perhaps of significance that the latter four physiological and pathological states and disease entities in which there is interstitial cell hyperplasia, are also characterized by an abnormality in steroid metabolism.

SUMMARY AND CONCLUSIONS

A case of interstitial cell tumor of the testis is reported. This is the first instance in which an interstitial cell tumor of the testis has been treated by local excision.

In this patient there was associated xanthoma formation and hypercholesterolemia. Evidence to suggest faulty steroidandrogen metabolism in disease of the interstitial cells is presented.

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REFERENCES

Butenandt, A. and Hanisch, G.: Ztschr. Physio. Chem., **237**: 89, 1935.
Chevassu, M.: Bull. et. Mém. Soc. Anat. de Paris, **82**: 684, 1907.
Friedman, N. B. and Moore, R. A.: Mil. Surg. **99**: 573, 1946.
Gilbert, J. W.: J. Urol., **44**: 345, 1940.
Glass, S. J., Edmonson, H. A. and Soll, S. N.: Endocrinol., **27**: 749, 1940.
Haines, J. S. and Grabstald, H.: Arch. Surg., **60**: 857, 1950.
Hansemann, D.: Arch. f. path. Anat., **142**: 538, 1895.
Huffman, L. F.: J. Urol., **45**: 692, 1941.
Kaufmann, E.: Deutsche med. Wchnschr., **34**: 803, 1908.
Marine, D.: Arch. Path., **28**: 65, 1939.
Masson, P. and Sencert, L.: Bull. de l'Assoc. franc. p. l'etude du cancer, **12**: 556, 1923.
Masson, P. and Venning, E. H.: Rev. Canad. de biol., **1**: 571, 1942.
Mathé, C. P.: J. Urol., **41**: 188, 1939.
Melicow, M. M., Robinson, J. N., Ivers, W. and Rainsford, L. K.: J. Urol., **62**: 672, 1949.
Reiners, C. R. and Horn, R. C.: Am. J. Clin. Path., **19**: 1039, 1949.
Rigoletti, L.: Arch. per le sc. med., **61**: 557, 1936.
Sharnoff, J. G. and Lisa, J. R.: J. Urol., **50**: 471, 1943.
Stewart, C. A., Bell, E. T. and Roehlke, A. B.: Am. J. Cancer, **26**: 144, 1936.
Waldeyer: Virch. Arch. f. path. anat. u Physiol., **55**: 67, 1872.
Warren, S. and Olshausen, K. W.: Am. J. Path., **19**: 307, 1943.

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BILATERAL INTERSTITIAL CELL TUMOR OF THE TESTICLE

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Interstitial cell tumors of the testicle have been an interesting, although rare, pathological entity. Many such cases so diganosed, including Waldeyer's original case in 1872, have instead been shown, in the light of recent pathological histological review, to be cases of hyperplasia. Authenticated cases of true tumor have not exceeded thirty.

Warren and Olshausen have given the following criteria for distinguishing between hyperplasia and tumor: "Hyperplasia—an increase of interstitial cells between the tubules without destruction or displacement of the tubules beyond the limits of the tumor." "Tumor—a discrete nodule or group of interstitial cells locally replacing or displacing the seminiferous tubules."

Melicow et al. have recently reviewed the literature and have added a case of tumor. Jemerin in 1937 presented an excellent review.

We wish to report what we believe to be the first American case of bilateral interstitial cell tumor and the second in the world's literature. Kaufmann's case, included in Melicow's review, of bilateral involvement has been generally accepted to be the only other such instance reported. (Rigoletti's case of 1936, included also in Melicow's review, has been shown to be unilateral rather than bilateral as reported.)

CASE REPORT

P. H. C. (No. 94042) aged 19, was originally seen in the out-patient department for a speech defect, a severe stutter. During his physical examination the incidental finding of bilaterally enlarged testicles was noted and he was referred to the urology clinic. The patient stated that he first noted enlargement of both testicles 5 years previously. There had never been any associated pain, trauma, or evidence of inflammation. The increase in size had been gradual, but had not lasted over a period of two or three months. He stated that before this time the testicles had been normal in size. Both testicles enlarged at the same time. The patient had developed slowly as a child and did not walk until the age of 2. He had always stuttered for as long as he could remember. He grew rapidly from the age of 6 to 12 years but since that time his size and weight had not changed appreciably.

The patient never had had more than a very slight interest in the opposite sex, as he stated it, "almost none." He had never had any "dates" and had had no hetero-sexual experiences. He had practiced masturbation occasionally although rarely He had never had any nocturnal emissions and stated that he had had no ejaculate with masturbation. The family history was interesting only in that a number of relatives stuttered.

Physical examination: The finding most immediately evident was the patient's stature (fig. 1). His trunk was stocky and the upper and lower extremities were shortened. The head was of normal size but gave the impression of relative increase in size, as compared with the trunk. The musculature was particularly well developed and was firm. The patient was mentally alert and apparently of normal average intelligence. He stuttered to an extreme degree. The positive physical findings were limited to those of the genitalia. The penis was considered to be of normal size. The testicles were enlarged bilaterally. The right testicle measured 8.8 by 5.5 by 4.5 cm. and the left was only very slightly smaller. Both were quite firm and were without nodules or tenderness. There was no transillumination. The vasa were smooth. The epididymis appeared to be normal except for a relative increase in size. The prostate was small, smooth and without nodules. Body measurements: height, 127.6 cm.; crown to symphysis, 63.8 cm.; symphysis to heel, 63.8 cm.; C 11 to L 4, 37.4 cm.; arm length, 50.6 cm.; thumb length, 5 cm.; forefinger length, 6.6 cm.; foot length 20.9 cm.; forearm length, 31.9 cm.; head circumference, 52.8 cm.; head transverse diameter, 14.3 cm.; distance from pupil to pupil, 5.5 cm.; distance from occiput to chin, 23 cm.; neck circumference, 34 cm.; chest circumference, expiration 71.5 cm.; inspiration, 73.5 cm.; waist, 62.7 cm.; hips, 59 cm.; biceps, 24.2 cm.; mid-thigh, 41.8 cm.; mid-calf, 29 cm. There was no gynecomastia.

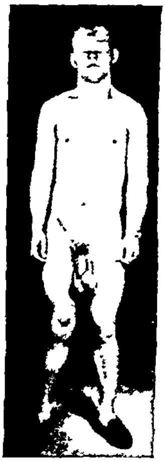

Fig 1. Photograph of patient. Note relatively shortened extremities

Blood examination showed 15 gm. hemoglobin and 5.4 million red blood cells and 7,900 white blood cells. Differential showed 48 polymorphonuclear leukocytes; 3 nonsegmented forms; 36 lymphocytes; 10 eosinophils; 1 monocyte; 2 basophiles. The urine was clear yellow, neutral in reaction, specific gravity 1.022. It was negative for albumin, sugar and casts. There was an occasional rare white blood cell. No red blood cells and no bacteria were seen on gram stain. The prostatic smear showed no spermatozoa and only an occasional white blood cell. The stool examination was negative for parasites, ova and occult blood. The Friedmann test was negative. Roentgen examination of the chest and of the skull showed no pathological changes. An excretory urogram showed a normal function bilaterally with normal pelves, calyces and renal shadows.

Bilateral testicular biopsy was performed on April 1, 1949. and microscopic sections taken immediately beneath the tunica albuginea revealed a few small, flat atrophic seminiferous tubules with a few spermatozoa within the lumina. Adjacent to these there were large sheets and irregular bands of polygonal cells which had abundant cytoplasm and a few granules. The nuclei were uniform in size generally, and an occasional few showed some degree of hyperchromatism. No seminiferous tubules were seen within the region of the large sheets of polygonal cells but only in the region immediately beneath the tunica albuginea. Pathological diagnosis at that time was "interstitial cell tumor of the testicle, bilateral."

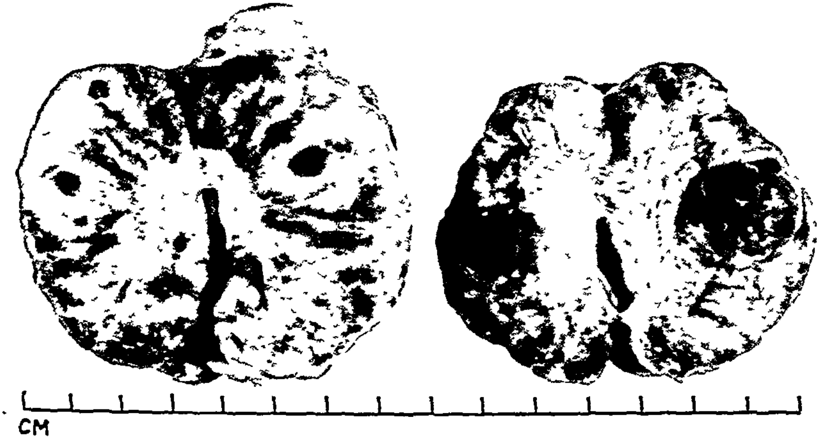

FIG 2 Cross section of gross specimens showing discrete tumor nodules. Right testicle is the larger

On April 5. 1949. under sodium pentothal anesthesia, a bilateral orchiectomy was performed. There was no evidence of extension of tumor. Each cord structure was divided at the level of the external inguinal ring. The right testicle measured 7 by 5 by 4 cm. and its surface was smooth: it was quite firm to palpation. It appeared to be of the same consistency throughout. On section there was no evidence of normal testicular tissue grossly (fig. 2). The tissue cut with a firm sensation There were scattered throughout the testicle dark brown. nodular areas of tissue discreetly separated from the stroma of the testicle. On sectioning the globus major, the same type of dark brown tissue was noted. The left testicle measured 6 by 4 by 3.5 cm., and it had the same firmness. On cross section the same dark brown tissue was seen. arranged in discrete nodules (fig. 2). There was one quite large and discrete nodule measuring 2 cm. in diameter. This projected above the cut surface of the remainder of the section. The epididymis was involved in a similar manner to that of the right side.

The same microscopic appearance was seen on either side. Sections taken through the brownish nodular tumor regions showed that the tumor was composed of irregular groups of large, oval or polygonal cells which had large, eccentrically located nuclei with quite prominent nucleoli. A number of cells had more than one nucleus. The cytoplasm was extensive and granular. The cells were arranged in large folds and sheets and very little fibrous tissue could be seen except in the regions surrounding the tumor borders. In sections taken immediately beneath the tunica albuginea a few atrophic tubules were seen. These showed no evidence of spermatogenesis. There were no interstitial cells intermingled among the atrophic compressed tubules. Mitotic figures were very rarely seen. No Reincke crystals were seen. No areas of necrosis or hemorrhage were noted. Sections taken near the right epididymis revealed compression in this area and as elsewhere there were great numbers of interstitial cells packed between fibrous acellular connective tissue. Sections through the globus major of the epididymis revealed sheets of interstitial cells as in the other areas, packed between fibrous connective tissue compressing the normal tubules of the epididymis. Occasionally large and bizarre nuclei were seen but for the most part the cells appeared entirely benign. Interpretation was "interstitial cell tumor of the testicle, bilateral." See figures 3, 4 and 5.

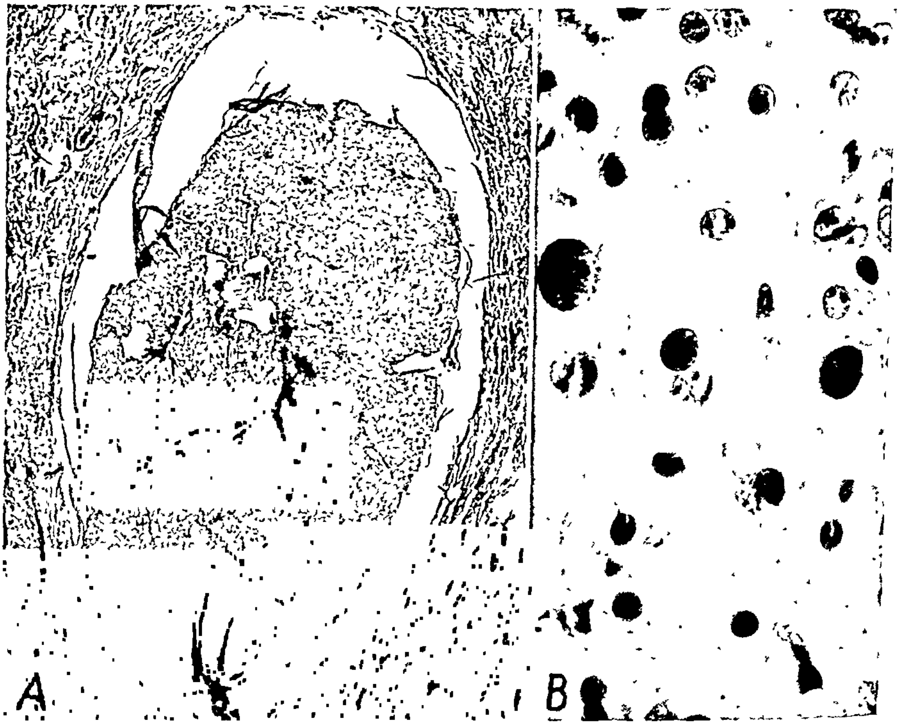

Fig. 3. *A*, microphotograph, × 4, showing discrete tumor nodule from testicle, right. *B*, microphotograph, × 300, of area of tumor nodule shown in *A*.

The postoperative course was uneventful and the patient was discharged on the second postoperative day. He was referred to the clinical psychologist for speech therapy. The prevalent opinion was that the microscopic picture showed no evidence of malignancy. It was for that reason that no deep roentgen therapy was given the patient.

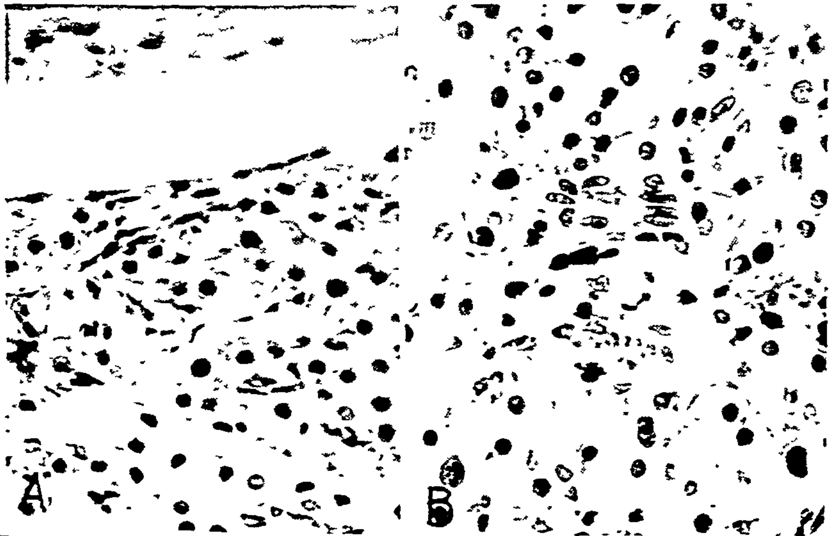

FIG. 4. *A*, microphotograph, × 145, from globus major, right, showing complete tumor involvement extending to tunica albuginea. *B*, microphotograph, × 145, from large tumor nodule in testicle, left.

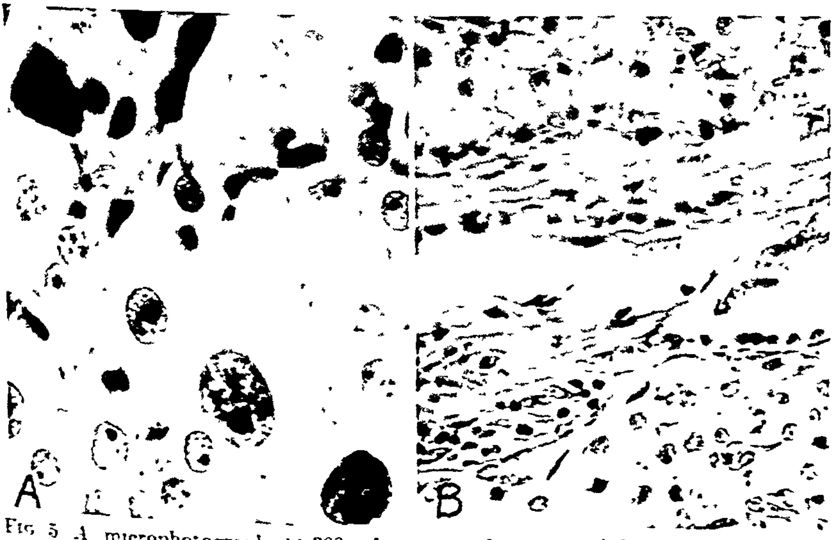

FIG. 5. *A*, microphotograph, × 300, of an area of tumor nodule shown in figure 4, *B*. *B*, microphotograph, × 145, from globus major, left, showing tumor cells on either side of strand of relatively acellular and partially hyalinized connective tissue.

He was seen several times in the clinic. The wound healed well bilaterally. His final checkup was on March 20, 1950, almost one year after his operation. He was completely asymptomatic and showed no clinical evidence of neoplastic growth. He was still receiving speech therapy. He stated that he had had no libido whatsoever since operation and had not practiced masturbation since that time. There was no change in the body stature.

DISCUSSION

A factor of greatest interest in this case is the endocrinological aspect. The patient, as can be seen in the photograph, presents an obvious variation in body stature. There was no gynecomastia. A careful history failed to uncover any evidence either of sexual precocity, either before or after puberty, or of increased libido following puberty. The case appears to be not one of gross hypergenitalism but of hypofunction. It seems to fit in fairly well with the majority of others reported of interstitial cell tumor developing after puberty. Hence one would not expect the changes seen in cases of tumor developing before puberty with their attendant sexual precocity.

It is somewhat confusing to attempt to correlate this case with others of interstitial cell tumor, especially those cases in which the tumor appeared prior to or at the onset of puberty, and in which marked sexual precocity was the rule. In our case, where the apparent onset of bilateral tumor occurred after the onset of puberty, there was never any sexual precocity, but rather more of a hypofunction in this regard. One would expect instead a hyperfunction in a tumor that manufactured testosterone. Melicow suggests that a possible explanation of this endocrinological dyscrasia may be that the tumor is a response to some unknown estrogenic influence. He cites the experiments of Bonser in which interstitial cell tumors resulted when male mice were given estradiol benzoate and triphenylethylene.

It generally has been believed that hyperplasia of the interstitial cells is accompanied by decreased spermatogenesis, as is true in our case, although the studies of Warren and Olshausen did not necessarily confirm this correlation.

Cases of proved malignancy accompanying interstitial cell tumor of the testicle have been only three in number, making this a quite rare complication. In relation to the total number of cases of tumor reported, however, malignancy could not be considered rare. Masson et al. have reported these cases. In view of the benign microscopic appearance of the tumor in our case, the decision to withhold roentgen therapy was made. The patient's course thus far has supported this decision.

SUMMARY

A case of bilateral interstitial cell tumor of the testicle in a 19 year old man has been reported. This is believed to be the first American case of bilateral involvement and the second case reported in the world's literature.

REFERENCES

Bonser, G. M.: J. Path. & Bact., **54**: 149, 1942.
Bonser, G. M. and Hawksley, L. M.: J. Path. & Bact., **55**: 295, 1943.
de Josselin de Jong, R.: Frankfurt. Ztschr. f. Path., **34**: 420, 1926.
James, D. C. and Shupe, R. D.: J. Urol., **63**: 718, 1950.

Jemerin, E. E.: Arch. Surg., 35: 967. 1937.
Masson, P. and Sencert, L.: Bull. d. l'Assoc. franc. p. l'etude du cancer. 12: 556. 1923.
Masson, P. and Venning, E. H.: Rev. Canad. de biol., 1: 571. 1942.
Melicow, M. M., Robinson, J. N., Ivers, W. and Rainsford, L. K.: J. Urol., 62: 672. 1949.
Nation, E. F., Edmondson, H. A. and Hammack, R. W.: Arch. Surg., 48: 415. 1944.
Neeve, R. H. and Marsh, F.: J. Path. & Bact., 56: 575. 1944.
Nelson, A. A.: Am. J. Path., 14: 831. 1938.
Price, I. L.: Brit. J. Surg., 36: 84, 1948.
Sharnoff, J. G. and Lisa, J. R.: J. Urol., 50: 471. 1943.
Stewart, C. A., Bell, E. T. and Roehlke, A. B.: Am. J. Cancer, 26: 144, 1936.
Warren, S. and Olshausen, K. W.: Am. J. Path., 19: 307, 1943.
Webber, F. P.: Lancet, 1: 1034, 1926.

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THE INFLUENCE OF HYPNOSIS ON SEMEN

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This study was undertaken in order to determine whether hypnosis can influence the production of semen, when secured in the absence of a sex partner. It was thought that emotional block might alter the collection of the maximum amount of semen, or reduce the total number of active sperm when the semen sample was secured by masturbation. Since hypnosis has been used to influence the functioning of the autonomic nervous system (Marcus) as well as for psychotherapy (Brenman), it appeared to be an appropriate experimental technique for the present purpose.

METHOD

Five subfertile married men were tested. The fertility of these persons was determined upon at least two examinations of semen by the method of Farris. The subjects were cooperative, of upper level in education and achievement, regarded as psychologically normal, and desirous of having children.

These men were interviewed in order to provide them with information about the procedure, and to give the observer an opportunity to test their reactions to suggestion. All of them were found to be susceptible to hypnosis.

Each individual was continent for five or more days before he supplied his sample of semen. Three subjects were hypnotized. A series of suggestions was made to each individual, directed toward the improvement of the semen sample. The details of the suggestions are omitted. The individual secured his semen sample in private. Following this, he was brought out of the hypnotic state. The fourth subject was hypnotized. He likewise was given suggestions toward improving the sample, following which he was brought out of the hypnotic state, and immediately supplied a sample. A week later he was hypnotized again, given a post-hypnotic suggestion towards improving the sample, and brought out of the hypnotic state. After a week of the post-hypnotic suggestion, he was hypnotized. He then secured a semen sample, in private. Following this he was brought out of the hypnotic state. The fifth man secured his first sample while he was in a hypnotic state, two hours after a post-hypnotic suggestion. One week later, while in a hypnotic state, a post-hypnotic suggestion was given. After 7 days, during which period this subject was continent and under the influence of a post-hypnotic suggestion, he was hypnotized. A sample of semen was secured in private, and he was brought out of his hypnotic state.

RESULTS

Note in line 5, table 1, that the number of active sperm in the total ejaculate was increased slightly from approximately 24 million to 39 million, during or following the hypnotic state, as compared with counts made before. In line 3 it

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This investigation was aided by a grant from the Samuel S. Fels Fund.

is seen that the number of active spermatozoa per cc. during and following the hypnotic state was higher than before, or from 7.5 to 10.5 million. The percentage of oval forms (line 9, table 1) increased from 58 to 81, during or following the hypnotic state.

TABLE 1. *Semen analyses of five subfertile men before, during and following the hypnotic state*

CHARACTERISTICS OF SEMEN	HYPNOTIC STATE			
	Before		During or Following	
	Av.	Range	Av.	Range
1. Volume of semen (cubic centimeters)	3.82	2.1–6.3	4.15	2.4–6.5
2. Active and inactive sperm per c.c. (millions)	18	3–35	32.9	5.5–52
3. Active sperm cells per c.c (millions)	7.5	1.5–12	10.5	1.5–22.5
4. Active and inactive sperm in total ejaculate (millions)	69.1	18.9–169	131.1	33.5–388
5. Active sperm in total ejaculate (millions)	24.3	17–43	39.0	9.1–67.5
6. Percentage of active sperm in total ejaculate	43	25–69	33.5	18–53
7. Speed of sperm (seconds)	1.2	1.1–1.5	1.33	0.9–1.8
8. Percentage of specimens active after 24 hours	1	0–5	1.4	1–2
9. Oval forms (percentage)	58	25–86	80.6	70–93

Averages are for the five individuals.

DISCUSSION

As a result of many other repeat studies of semen of men (Farris), it has been ascertained that the normal degree of variation from time to time could explain the differences in the findings during and following the hypnotic state. Therefore, the findings indicate that hypnosis has little if any effect upon the characteristics of semen.

CONCLUSIONS

It is possible for men to produce and secure semen samples for examination while under hypnosis.

In this experiment, the hypnotic state had no significant influence upon the characteristics of the semen.

REFERENCES

BRENMAN, M. AND GILL, M. M.: Hypnotherapy. New York: Josiah Macy, Jr., Foundation, 1944

FARRIS, E. J. Human Fertility and Problems of the Male. Palisades Park, N. J.: The Author's Press, 1950.

MARCUS, H. AND SAHLGRAN, E.: 1936. Untersuchungen über die Einwirkung der hypnotischen Suggestion auf die Funcktionien des vegetatinen Systems. Acta Psychiat. et Neurol., 11: 119–126, 1936. (Abstract.)

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PRELIMINARY REPORT ON USE OF TETRAZOLIUM CHLORIDE IN GENITO-URINARY CANCER

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The demonstration of reducing enzyme systems in plants and living mammalian tissues by triphenyltetrazolium chloride has been reported in the litera-

Table 1

TISSUE	SOLUTION	pH	TIME	TEMP. ROOM	RESULTS
			min.		
1. Human kidney. Carcinoma of kidney. Cut surface of surgical specimen.	1%	5.5	30	37°	Deep violet staining of normal parenchyma, none of the neoplasm.
2. Human kidney. Carcinoma of kidney. Cut surface of surgical specimen.	1%	5.5	35	37°	Deep violet staining of normal parenchyma, none of the neoplasm.
3. Human kidney. Carcinoma of kidney. Cut surface of surgical specimen.	1%	5.5	35	37°	Deep violet staining of normal parenchyma, none of the neoplasm.
4. Human kidney. Wilms' tumor. Cut surface of surgical specimen.	1%	5.5	35	37°	Deep violet staining of normal parenchyma, none of the neoplasm.
5. Human kidney. Epidermoid carcinoma. Cut surface of surgical specimen.	¼%	7.2	40	37°	Deep violet staining of hydronephrotic parenchyma, none of neoplasm.
6. Carcinoma of penis. Surgical specimen. Surface of neoplasm.	¼%	7.2	30	37°	Deep violet staining of carcinoma
				TEMP. PATIENT	
7. Carcinoma of urethra. Female, living specimen.	¼%	7.2	20	98.6	Violet staining of neoplasm none of surrounding tissue
8. Carcinoma of bladder in exstrophy, living subject.	¼%	7.2	35	99.2	Violet staining of neoplasm none of "normal" bladder epithelium
9. Carcinoma of bladder. Living subject.	20 cc of ¼% solution instilled in bladder	7.2	50	98.8	Violet staining of neoplasm none of normal bladder epithelium

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ture.[1, 2, 3, 4] Straus, Cheronis, and Straus[5] reported observations on neoplastic and living mammalian tissues and included three clinical observations. Two cases of carcinoma were stained differentially from surrounding tissue and in another case an area of granulation tissue was not.

Solutions of tetrazolium salts are reduced to colored formazan when in contact with certain reductases in living tissue.

Using 1 per cent and $\frac{1}{4}$ per cent solutions of triphenyltetrazolium, violet, in physiological normal saline, applications in cotton gauze were made to fresh surgical specimens and to lesions in living subjects. Table 1 indicates results of preliminary studies.

The use of this compound is applicable to many avenues of investigations and clinical use. Metabolism of normal and neoplastic genito-urinary tissues, detection of small areas of neoplasia in surgical specimens, in suspicious lesions of the penis, urethra, and bladder are a few. Cystoscopic aid is particularly intriguing.

A further report is contemplated when a larger series of cases is accumulated.

[1] Lakon, G.: Ber. deutsch. bot. Gesellsch. **60:** 299, 434, 1942.

[2] Porter, H. R., Durrell, M. and Romm, H. J.: Plant. Physiol., **22:** 149, 1947.

[3] Stein, R. J. and Gerarde, H. W.: Science, **111:** 591, 1950.

[4] Jensen, C. O., Sacks, W. and Baldanski, F. A.: Science, **113:** 65, 1951.

[5] Straus, F. H., Cheronis, N. D. and Straus, E.: Science, **180:** 113, 1948.

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THE USE OF FORMALIN AND ALCOHOL IN THE ESTIMATION OF PROSTATIC PHOSPHATASE

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Since Gutman and his colleagues[1] drew attention to the increase of serum acid phosphatase in metastasizing prostatic carcinoma, a large number of reports have appeared confirming and extending their observations. Among other workers, the contributions of Huggins and his school[2] have proved to be particularly fruitful and, at the present time, there is fairly general agreement about the value and limitations of the estimation of serum acid phosphatase not only in the diagnosis but also in following the stilbestrol treatment of prostatic cancer.

Although evidence has been accumulating for some time that several different acid phosphatases may be present in the blood stream in various circumstances only one of which is derived from the prostate gland, early workers did not, or were unable to, distinguish between them.

Recent work, however, has drawn attention to important differences in the behavior of the different enzymes, and attempts can now be made to develop methods for estimating the prostatic enzyme in the presence of other enzymes in the acid phosphatase group. Herbert,[3] for example, has tried two procedures, one based on the fact that prostatic phosphatase is irreversibly inactivated by alcohol and the other on the observation that prostatic phosphatase is more easily destroyed by incubation at 37° than is the normal serum component. Another approach has been made by Abul Fad'l and King[4] who have reported the interesting observations that formaldehyde in optimum concentration has no effect on the prostatic enzyme, but completely destroys that of the red cell; other phosphatases tend to be inhibited.

It seems reasonable to suppose that, if it were possible to have a method for determining acid phosphatase concentration in the serum which would be specific for the prostatic enzyme, such a method would be of considerable value in clinical practice, especially under those circumstances where existing procedures give "border line" results.

In applying her methods, Herbert came to the conclusion that, while her method of incubating the serum at 37° was of little value, in routine diagnostic work, her alcohol procedure gave an approximate measure of the prostatic fraction of the serum acid phosphatase. From a study of 102 sera in nonprostatic disease, she found only two exceptions to the rule that treatment with alcohol under her conditions does not cause a fall of more than 1 unit per 100 ml. of serum.

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[1] Gutman, E. B. Sproul, E. E. and Gutman, A. B.: Am. J. Cancer, **28:** 495, 1936.
[2] Huggins, C. and Hodges, C. V.: Cancer Res., **1:** 293, 1941.
[3] Herbert, F. H.: Quart. J. Med., **59:** 221, 1946.
[4] Abul Fad'l, M. A. M. and King, E. J.: J. Clin. Path., **1:** 80, 1948.

Abul Fad'l and King applied their formalin technique to a fairly large series of cases and claimed that the procedure provided useful information for distinguishing in many cases between raised values due to the presence of prostatic phosphatase and those of different origin, while Herbert's alcohol method gave further confirmatory evidence in doubtful cases.

A consequence of the fact that formalin completely destroys the red cell phosphatase is that hemolyzed sera, which would otherwise be useless for phosphatase estimation, may be used. The practical value of this observation has been demonstrated by Benseley, Wood and Lang[5] and confirmed by ourselves.

Simultaneously with an investigation of the kinetics of the various phosphatases, we thought it would be interesting to study the uses of the formalin and alcohol methods. This paper reports our conclusions after a study of 336 cases.

CLINICAL STUDIES

Our approach to this problem has been the essentially practical one of assessing the value of the inactivation techniques at present available in clinical practice.

Samples of blood were taken, in the main, from hospital patients and the separated serum was analyzed for alkaline phosphatase, and for total alcohol active, and formalin stable phosphatases.

In the selection of samples for analyses, our general procedure was to utilize all blood samples on which phosphatase determination was requested as a routine investigational procedure. This naturally provided a large number of cases with disease of the prostate on which acid phosphatase was needed and a further series in which alkaline phosphatase was required to assist in the differential diagnosis of liver disease or bone conditions. In order to supplement these numbers, and to balance the survey, a special effort was made to examine samples 1) from other cases (especially those in which raised phosphatase values might be expected) and 2) to study a series of healthy men, medical students, and staff members who served as normal controls.

All estimations were carried out as soon as possible after collection, usually within a few hours. Although we aimed at the estimation of alcohol-active and formalin-stable enzyme as well as total phosphatase on all our cases, sometimes this was not technically possible with the volumes of serum available. In this situation priority was given to the total and formalin procedures, since for reasons adduced in a later part of this paper, we feel that the alcohol procedure is of more limited value, and we regarded it as more important to estimate one or more of the fractions in duplicate rather than to estimate all of them singly.

The diagnosis of prostatic carcinoma was made by rectal examination, the presence of bony metastases or the pathological studies of surgical biopsies. Confirmation was obtained by histological studies in all but two of the cases

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[5] Benseley, E. H., Wood, P. and Lang, D.: Am. J. Clin. Path., 18: 742, 1948.

(Nos. 9 and 10) and in these, rectal examination was strongly suggestive of the diagnosis.

X-ray examination of the chest, lumbar spine and pelvis was carried out as a routine on all patients found to have prostatic cancer.

The *diagnosis of benign prostatic hypertrophy was confirmed by histological* studies in all but 3 cases and in these, no carcinoma was felt on rectal examination.

Other carcinomas were diagnosed by histological examinations only after careful rectal examination for a clinically apparent carcinoma of the prostate gland.

In the jaundice cases, clinical observations were supplemented by the following tests of liver function serum bilirubin, alkaline phosphatase thymol turbidity, and cephalin flocculation.

LABORATORY PROCEDURES

The following explains the terms given to the various phosphatase fractions and indicates the methods by which they were determined.

Total acid phosphatase, the value obtained by the usual procedure without the use of any inhibiting substance. The method was that previously described[6] in which the substrate is phenyl phosphate and the hydrolysis was allowed to proceed for one hour at 37° in the presence of citrate buffer of pH 4.9.

Formalin-resistant acid phosphatase is the residual phosphatase activity in the presence of formalin under the conditions of Abul Fad'l and King. Briefly the procedure is to set up another test in which 2 per cent formalin is incorporated in the incubation mixture and to estimate this side by side with the total enzyme determination.

Alcohol-active acid phosphatase is the acid phosphatase activity exhibited after treatment with alcohol under the conditions of Herbert. This term is to be preferred to alcohol-stable acid phosphatase since treatment with alcohol often leads to an increase in activity.

Essentially the method consists of a preliminary incubation of 1 ml. of the serum with 0.4 ml. of absolute alcohol at 37° for one hour. An aliquot of the incubated mixture is then analyzed by the total acid phosphatase procedure.

RESULTS

In addition to the complete table of findings given in the appendix,* the values obtained for total and formalin resistant acid phosphatase are analyzed in table 1 and illustrated by the charts (figs. 1 and 2) while the effect of alcohol is analyzed in table 2. In every case the findings are grouped according to the disease. The use of stilbestrol is so well established as a therapeutic measure nowadays that some of our patients with prostatic cancer had already been treated in this manner before coming to hospital. Since we were concerned with the study of results as they were obtained in practice, it was decided to include these patients. In the tables, therefore, our findings are subdivided into those patients who had had endocrine therapy before the phosphatase estimation and those who had not. It should also be mentioned that most of the men who had been treated with stilbestrol were not adequately controlled, since the presenting symptoms were in the majority of the cases related to their prostatic carcinoma.

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[6] Delory, G. E.: Estimation of Serum Phosphatase; Photoelectric Methods in Clinical Biochemistry, pp. 57, Hilger and Watts, Ltd., London, (1949).

* The appendix will be found in the authors' reprints. *Editor.*

TABLE 1. *Unbracketed figures show total, bracketed—formalin stable acid phosphatase*

CONDITIONS	NUMBER OF CASES	SERUM PHOSPHATASE (Units per 100 ml.)																			
		0.0 to 1.0	1.1 to 1.5	1.6 to 2.0	2.1 to 2.5	2.6 to 3.0	3.1 to 3.5	3.6 to 4.0	4.1 to 4.5	4.6 to 5.0	5.1 to 5.5	5.6 to 6.0	6.1 to 6.5	6.6 to 7.0	7.1 to 7.5	7.6 to 8.0	8.1 to 8.5	8.6 to 9.0	9.1 to 9.5	9.6 to 10.0	More than 10.0
1) *Carcinoma of prostate with bone metastases*																					
a) No endocrine therapy before phosphatase estimation	12 (11)	0 (0)	1 (1)	0 (0)	0 (0)	0 (1)	1 (0)	0 (0)	0 (0)	0 (0)	1 (0)	0 (0)	0 (0)	0 (0)	1 (1)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	8 (8)
b) Some endocrine therapy before phosphatase estimation	11 (11)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (2)	2 (1)	1 (0)	0 (0)	1 (1)	0 (1)	0 (0)	1 (0)	2 (2)	0 (1)	1 (1)	0 (0)	0 (0)	0 (0)	3 (2)
2) *Carcinoma of prostate without bone metastases*																					
a) No endocrine therapy before phosphatase estimation	18 (17)	0 (3)	1 (2)	0 (0)	6 (4)	1 (1)	2 (0)	0 (0)	0 (2)	1 (1)	1 (0)	1 (2)	2 (0)	0 (0)	0 (0)	0 (0)	0 (1)	1 (0)	0 (0)	1 (0)	1 (1)
b) Some endocrine therapy before phosphatase estimation	9 (9)	0 (1)	0 (1)	0 (3)	3 (0)	3 (1)	0 (0)	6 (1)	1 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0)						
3) *Benign prostatic hypertrophy*	94 (94)	1 (9)	5 (9)	6 (10)	11 (22)	14 (12)	17 (6)	8 (10)	13 (2)	8 (7)	2 (3)	2 (3)	2 (1)	2	1	0	0	2			
4) *Cancer other than that that of prostate*	29 (29)	0 (2)	1 (0)	2 (8)	2 (7)	3 (4)	6 (3)	6 (3)	1 (1)	3 (0)	1 (0)	2 (1)	1	0	0	1					
5) *Diseases of liver and bile tract*	36 (36)	0 (0)	1 (3)	2 (2)	0 (3)	2 (8)	8 (4)	3 (3)	4 (3)	3 (3)	1 (2)	4 (2)	1 (1)	1 (0)	3 (1)	1 (1)	1	0	1		
6) *Diseases of kidney*	12 (12)	0 (1)	1 (1)	0 (2)	1 (4)	1 (0)	2 (1)	3 (2)	2 (1)	0	0	1	0	1							
7) *Paget's disease of bone*	9 (9)	0 (0)	2 (3)	0 (1)	2 (0)	1 (3)	2 (0)	0 (1)	0 (0)	1 (0)	0 (1)	0 (0)	0 (0)	1							
8) *Miscellaneous diseases*	29 (29)	0 (1)	2 (6)	3 (9)	5 (5)	3 (4)	3 (0)	5 (3)	1 (1)	2	2	1	1	1							
9) *Healthy subjects*	77 (77)	0 (1)	0 (14)	5 (16)	3 (19)	7 (15)	15 (8)	21 (2)	18 (11)	6 (0)	2 (1)										
Total	336 (334)																				

DISCUSSION

It will be convenient in the first instance to discuss the findings in each group separately.

Healthy males. Seventy-seven people were studied. The range for total acid phosphatase was 1.8–5.3 units, giving a mean of 3.6 with a standard deviation of 0.79. The corresponding figures for the formalin-resistant enzyme were 0.7–5.1 units with a mean of 2.3 and a standard deviation of 0.74.

The findings for total enzyme are in agreement with those of others who have used similar methods. So far as we know, however, there has been no extensive comparable survey of normal males but our figures support the statement of Abul Fad'l that a value above 5 units per 100 ml. strongly suggests that the increased enzyme content of the serum studied is of prostatic origin while a value greater than 3 is "suspicious".

TABLE 2. *Effect of alcohol on serum acid phosphatase*

Values expressed as units per 100 ml.

CONDITION	NUMBER OF CASES	−2.0 to −1.6	−1.5 to −1.1	−1.0 to −0.6	−0.5 to −0.1	±0 to +0.5	+0.6 to +1.0	+1.1 to +1.5	+1.6 to +2.0	MORE THAN +2.0
1) *Carcinoma of prostate with bone metastases*										
a) No endocrine therapy before phosphatase estimation . .	2	0	0	0	1	0	1	0	0	0
b) Some endocrine therapy before phosphatase estimation	4	2	0	0	0	1	0	0	0	1
2) *Carcinoma of prostate without bone metastases*										
a) No endocrine therapy before phosphatase estimation	10	2	0	2	3	1	0	1	1	0
b) Some endocrine therapy before phosphatase estimation	6	1	0	1	3	0	1	0	0	0
3) *Benign prostatic hypertrophy*	36	2	2	6	11	6	5	3	1	0
4) *Cancer other than of the prostate*	11	1	0	5	4	1	0	0	0	0
5) *Diseases of liver and bile tract*	17	1	3	4	6	1	2	0	0	0
6) *Diseases of kidney*	9	1	1	2	2	1	2	0	0	0
7) *Paget's disease of the bone*	7	0	0	0	5	0	1	0	1	0
8) *Miscellaneous diseases*	14	0	3	5	0	2	1	2	0	1
9) *Healthy subjects*	70	2	12	9	8	30	5	2	1	1
Total	186	12	21	34	43	43	18	8	4	3

Of the 77 cases studied in this group, Herbert's procedure was carried out in 69 of them. There were 13 exceptions to Herbert's rule that in nonprostatic disease, alcohol does not produce a drop of more than 1 unit per 100 ml. The greatest fall in our series was 1.8 units. It has to be borne in mind, of course, that the amounts determined are very small and are approaching the limit of accuracy of the method.

Prostatic cancer with demonstrable bone metastases. As already mentioned, this group is subdivided according to whether the patient had or had not been subjected to endocrine therapy before the phosphatase levels were determined. In view of the possible effect of the treatment on the enzyme concentrations, only the untreated cases will be discussed here. Twelve cases were studied for total acid phosphatase, of which 10 were greater than the accepted upper limit of normal of 5 units per 100 ml. This is in general agreement with the findings of other workers. It has been suggested that the low figures found from time to time in undoubted metastasing prostatic cancer may be due to the presence of a tumour of the anaplastic type but we have not found any evidence of this in our series.

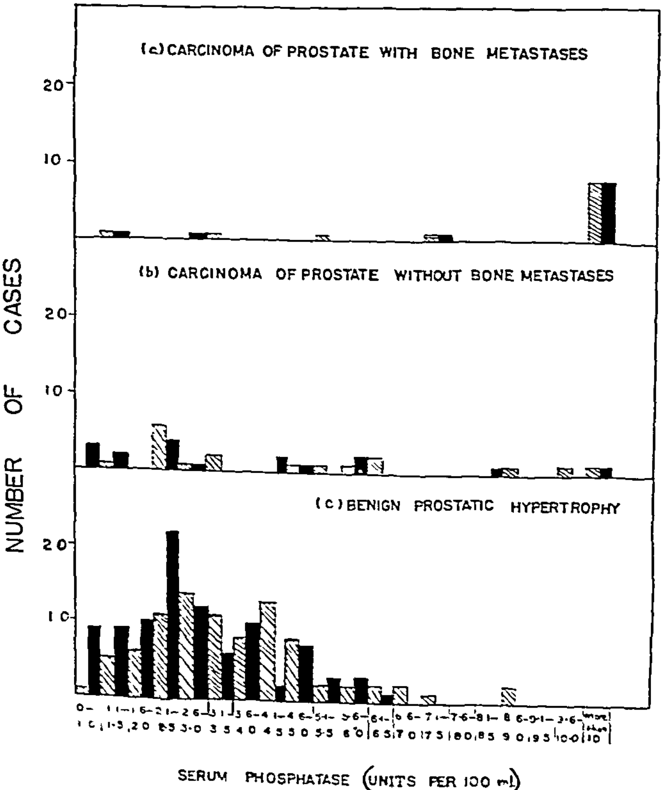

FIG 1. Showing distribution of serum acid phosphatase values among following groups: a) carcinoma of prostate with demonstrable bone metastases; b) carcinoma of prostate without demonstrable bone metastases; c) benign prostatic hypertrophy. Hatched areas represent total; blocked, formalin resistant phosphatase.

Of the 11 cases where the formalin-resistant enzyme was determined, 9 were greater than 5 units per 100 ml. None was between 3 and 5 units:

Herbert's alcohol procedure was carried out on 6 of the cases, 4 showing a fall after addition of alcohol of more than 1 unit per 100 ml. The two other cases, one of which gave a fall of 0.5 and the other a rise of 0.7 units per 100 ml., were associated with total acid phosphatase values of 5.2 and 3.5 respectively.

Prostatic cancer without demonstrable metastases. Of the 18 cases studied for total acid phosphatase in the untreated group, 7 gave results higher than 5 units per 100 ml. In 17 of these, the formalin-resistant enzyme was estimated and of these 4 gave figures greater than 5 units per 100 ml. and 3 others were between 3.0 and 5.0.

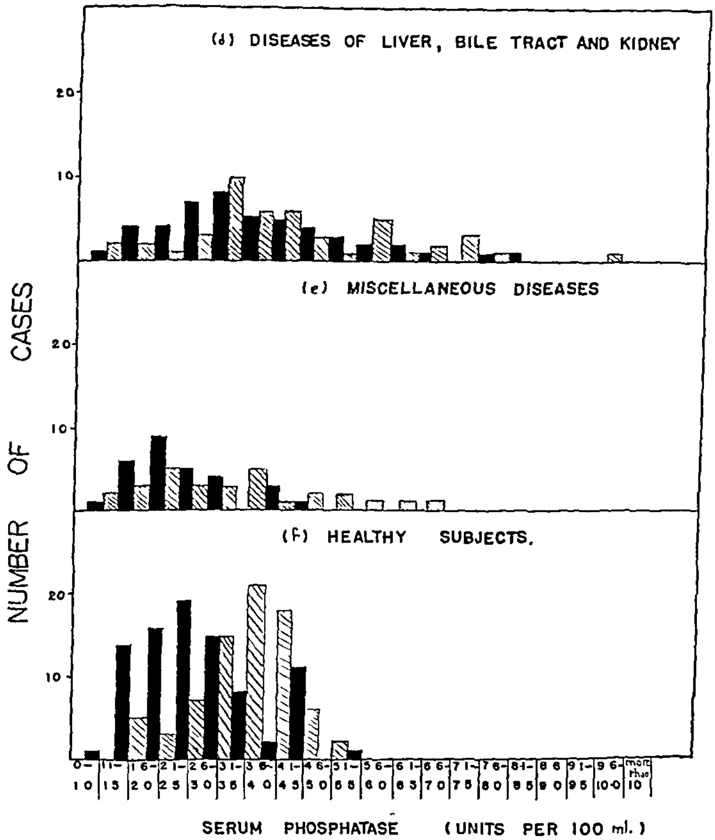

FIG. 2. Showing distribution of serum acid phosphatase values among following groups: d) diseases of liver, bile tract and kidney; e) miscellaneous diseases, and f) healthy subjects.

Eleven patients were examined for alcohol-active acid phosphatase and of these only 3 exhibited falls after alcohol treatment greater than 1.0 units per 100 ml. In 5 of the remaining cases in the series, (that is where there was a rise in activity after treatment with alcohol or where the fall was less than 1.0 unit per 100 ml.), the total acid phosphatase was within the normal range. In one case, there was a fall of 0.7 units with a total acid phosphatase of 6.1 units.

Benign prostatic hypertrophy. Total acid phosphatase was estimated on 95 cases. Of these 12 gave results greater than 5 units per 100 ml. but in only one of these, which has been previously reported in detail (Stewart, Sweetser and Delory[7]), was the value greater than 9 units per 100 ml. In this case, the phosphatase fell to within normal limits after prostatectomy and histological examination showed the presence of a recent infarct. It is possible that under these conditions a channel had been set up which enabled the enzyme to leak from the prostatic gland into the blood stream.

The formalin procedure was carried out on 95 cases. Apart from the case with the recent infarct mentioned above, there were 7 values greater than 5 units per 100 ml. and 32 greater than 3 units per 100 ml.

Alcohol-active enzyme was determined in 42 of the patients; of these 10 gave falls after alcohol treatment greater than 1.0 unit per 100 ml.

Nonprostatic diseases. Since the findings for the various groupings are given in table 1 they may be considered together here.

Total acid phosphatase values greater than 5 units per 100 ml. were obtained in 5 out of 29 cases of cancer other than of prostate, 13 out of 36 in diseases of liver and bile tract, 2 out of 12 diseases of kidney, 1 out of 9 in Paget's disease of bone and 5 out of 29 miscellaneous diseases.

A method for the differential estimation of acid phosphatase might be expected to be most useful in those circumstances where the total enzyme content is raised and it is desired to know which component is responsible for the increase. The alternative, namely, to locate an increased amount of a particular acid phosphatase in a sample showing a normal total enzyme content seems less hopeful at the present stage of our knowledge. According to Herbert, raised total values are most frequently to be found (if we exclude prostatic cancer) in diseases of the liver and kidney; 2 out of her 16 cases of nephritis and 8 out of her 20 cases of liver disease giving total acid phosphatase values greater than 5 units per 100 ml. The corresponding figures of Abul Fad'l and King were, 6 out of 16 and 22 out of 38. None of Herbert's results were higher than 8 units per 100 ml. while Abul Fad'l and King's highest figure was 12 in nephritis and 19 in obstructive jaundice. Our figures are 1 out of 10 in diseases of the kidney and 12 out of 36 in liver disease.

Abul Fad'l and King also found a number of very high results in their miscellaneous group, the highest being 24 in a case of bronchopneumonia. The highest in the corresponding group of our series is 6.9 units per 100 ml.

To facilitate examination of the formalin and alcohol methods in assessing abnormally high total phosphatase figures, table 3 shows all the cases in which we obtained total serum acid phosphatase values greater than 5 units per 100 ml. together with the other findings in the cases.

It will be seen that, if we accept 5 units as the upper limit for the formalin-resistant enzyme, the number of high values is reduced although by no means eliminated. Out of 37 cases other than prostatic carcinoma where the total acid phosphatase is raised, the formalin resistant enzyme is greater than 5 units per 100 ml. in 16 cases and between 3 and 5 units per 100 ml. in 18 cases.

So far as the alcohol procedure is concerned, 16 cases showed raised total phos-

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[7] Stewart, C. B., Sweetser, T. H. Jr. and Delory, G. E.: J. Urol., 63: 128, 1950.

Table 3. *Cases other than prostatic cancer in which total acid phosphatase was greater than 5 units per 100 ml.*

NUMBER OF CASE	TOTAL	ALCOHOL ACTIVE	EFFECT OF ALCOHOL FALL − RISE +	FORMALIN STABLE	ALKALINE
a) Benign prostatic hypertrophy					
63	6.1	3.6	−2.5	5.6	10.7
86	124.0	—	—	116.0	13.2
89	5.1	—	—	2.6	8.4
102	5.7	—	—	4.6	16.0
106	8.9	—	—	4.9	—
107	7.3	—	—	3.6	—
111	8.8	—	—	4.7	—
113	6.9	—	—	5.8	11.2
114	5.3	—	—	4.1	6.5
122	6.3	—	—	5.2	—
124	6.9	—	—	4.0	—
153	5.8	−0.7	−5.1	5.8	11.7
b) Cancer other than of prostate					
160	5.4	5.3	−0.1	3.5	10.3
166	5.6	3.6	−2.0	3.0	7.5
174	6.1	—	—	5.6	11.6
175	5.7	—	—	4.5	—
180	8.5	—	—	2.0	59
c) Diseases of liver and bile tract					
201	5.5	5.5	—	5.0	27.9
202	6.2	6.0	−0.2	4.6	15.0
203	9.2	—	—	7.3	17.3
204	5.6	3.8	−1.4	4.2	32.8
206	7.5	—	—	5.8	78
208	8.1	—	—	3.8	28.5
209	5.7	—	—	1.2	14.0
211	7.6	—	—	7.6	116
213	7.4	—	—	6.3	24.6
221	6.8	5.2	−1.6	5.3	27.2
234	5.9	5.6	−0.3	4.9	30.2
235	5.7	4.8	−0.9	3.4	17.0
236	7.5	6.5	−1.0	5.5	39.0
d) Diseases of the kidney					
251	6.5	5.2	−1.3	4.4	13.0
e) Paget's disease of the bone					
272	6.9	—	—	5.2	11.7
f) Miscellaneous diseases					
300	5.1	—	—	4.0	—
301	6.4	—	—	2.4	—
302	5.2	—	—	1.2	5.2
307	6.0	—	—	1.6	—
316	6.9	3.5	−3.4	4.5	9.2

phatase values and of these 9 violated Herbert's rule that in nonprostatic disease the fall on treatment with alcohol should not be greater than 1.0 unit per 100 ml. This is a much less sharp differentiation than Herbert found but more like that of Abul Fad'l and King. Taking the latter's miscellaneous group as an example, out of 73 cases, 22 gave total acid phosphatase values greater than 5 units per 100 ml., 6 gave raised formalin values. Of these 22 cases the alcohol was carried out on 13, the fall after treatment with alcohol being greater than 1 unit in 7 of them.

It seems, therefore, that the use of the proposed methods for distinguishing between the various components of the serum acid phosphatase is somewhat limited at the present state of our knowledge. However, the simplicity of the formalin method and the fact that errors due to the blood being hemolyzed are eliminated entitles it to a place in the routine clinical laboratory.

SUMMARY

The total and formalin resistant serum acid phosphatase concentration has been determined on 77 healthy individuals and 259 hospital patients and the effect of 40 per cent alcohol on the serum acid phosphatase level has been studied with 116 hospital patients and 70 healthy individuals.

In the healthy males, the range for total acid phosphatase was 1.8–5.3 units per 100 cc. giving a mean of 3.6 with a standard deviation of 0.79, while the corresponding figures for the formalin resistant enzyme were 0.7–5.1 units with a mean of 2.3 and a standard deviation of 0.74.

The effect of alcohol on the serum acid phosphatase among the healthy individuals was variable. In 56 per cent of the cases, a fall of activity down to −2.0 was found while in the remaining cases the activity was either unchanged or increases, the highest increase encountered being 2.1.

The formalin procedure proved useful in elucidating the diagnosis in some cases where the total estimation gave misleading results, but it was not uniformly successful.

Nevertheless, the simplicity of the formalin technique, the elimination of errors due to hemolysis and the higher significance of the values obtained earn it a place in the routine clinical laboratory.

Grateful thanks are due to all those clinicians of both the Preston Royal Infirmary and the Winnipeg General Hospital especially Mr. W. H. Graham of Preston and Dr. C. B. Stewart of Winnipeg who permitted us to study patients in their care, and for their helpful discussions of the clinical aspects. Dr. J. M. Kilgour of Winnipeg advised us on some of the medical questions.

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NEW USES FOR THE WAX TIP

JOHN K. ORMOND

From the Henry Ford Hospital, Detroit, Mich.

For years it has been our custom to use the wax tipped bougie or catheter in the diagnosis of ureteral calculi. On several occasions in which the wax tipped bougie passed up the ureter with ease, I found that the ordinary ureteral catheter met obstruction lower in the ureter than the stone, and that in such instances dipping the end of the catheter in melted wax often permitted easy passage of the catheter. I thought it probable that the end of the catheter, in these instances, caught in the lining membrane of the ureter, and that the smooth coating of wax prevented this. It occurred to me that this might be a useful procedure in cases of urethral stricture through which filiforms were passed with difficulty, and I have used the method with great satisfaction since then.

In cases in which the filiform lodges in the face of the stricture, I make a small wax bulb on its end. In many cases it will then pass. I presume that there may be fissures or pockets in the face of the stricture in which the bare end of the filiforms may lodge, but over which the smooth little wax bulb passes. However, I have on occasion had to use two or three filiforms so prepared, simultaneously. Probably a small pit or fissure was filled by one of the wax bulbs allowing another to pass.

This little procedure not only saves time but diminishes the discomfort of the patient.

MEETING, NEW YORK SOCIETY OF THE AMERICAN UROLOGICAL ASSOCIATION

November 14, 1951

Yale Club, New York City

8:30 P.M. PAPER OF THE EVENING:

Dr. David M. Davis, Professor of Urology, Jefferson Medical College, Philadelphia

DISCUSSION: Dr. Clyde C. Deming, New Haven; Dr. John N. Robinson, New York City

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RENAL TUBERCULOSIS WITH ADDISON'S DISEASE

WILLIAM J. ENGEL, RICHARD S. GRAVES AND ROBERT W. SCHNEIDER

From the Cleveland Clinic and the Frank E. Bunts Educational Institute, Cleveland, Ohio

Chronic adrenal insufficiency results from slowly progressive destruction of the adrenal cortex and was first described by Thomas Addison in 1855. One of the common causes is tuberculosis of the adrenals but in many cases it results from unexplained atrophy of the gland. Gummas, metastases, hemorrhage, infarction and amyloidosis have been implicated. Rowntree[1] reports that it occurs twice as often in men as in women. However, a review of 66 cases at the Cleveland Clinic reveals that 34 were men and 32 were women. According to the Census Bureau it is responsible for 0.4 deaths per 100,000.

Addison's disease may co-exist with renal tuberculosis and it is important that it be recognized. The symptoms of Addison's disease are often quite vague and may closely resemble those produced by any debilitating disease such as renal tuberculosis. For that reason the urologist may not consider adrenal insufficiency when evaluating or treating urogenital tuberculosis. Such things as weakness, anorexia, weight loss, dizziness, faintness and fatigue might easily be attributed to tuberculosis. Arterial hypotension and a craving for salt are more suggestive of depressed adrenal function. A characteristic pigmentation of the skin and mucous membranes may be seen in Addison's disease, but does not always occur. Boyd[2] cites a case in which prolonged bed rest for osseous tuberculosis obscured the weakness and exposure to sunlight masked the pigmentation.

Once the urologist suspects that a case of renal tuberculosis is complicated by adrenal cortical deficiency the diagnosis can usually be made on clinical grounds. However, there are a number of laboratory tests which may be helpful in confirming the diagnosis. The blood sodium may be reduced and the urea, nonprotein nitrogen and potassium may be increased. However, blood electrolytes are frequently normal even in crisis. The Kepler water excretion test may be of value in indicating the presence of Addison's disease. False positive tests must be differentiated,[3] however. The urinary 17-ketosteroids are reduced and in women there may be practically none since it is generally believed that the adrenal is the only source of 17-ketosteroids in the female.[4] Determination of the circulating eosinophils and urinary uric acid in the manner described by Thorn[5] may be employed. In the subject with an intact adrenal cortex there will be a decrease in the eosinophil count and an increase in the urinary uric acid after injection of adrenocorticotropic hormone. Roentgen examination may show calcification of one or both adrenals. Biopsies of pigmented areas will reveal melanin

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Read at annual meeting, North Central Section, American Urological Association, Milwaukee, Wis., October 12, 1950.

[1] Rowntree, cited by Cecil: A Text of Medicine.

[2] Boyd, M. L.: Tr. Am. A. Genito-Urin. Surg., 35: 235, 1943.

[3] Schneider, R. W.: Cleveland Clin. Quart., 11: 22, 1944.

[4] McCullagh, E. P., Schneider, R. W., Bowman, W. and Smith, M. B.: J. Clin. Endocrinol., 8: 275, 1948.

[5] Thorn, G. W.: J. A. M. A., 137: 1005, 1948.

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A week later cystoscopic study revealed multiple small ulcerations in the bladder but no evidence of ureteral stricture on catheterization The left kidney presented a normal pyelogram In the right pyelogram the superior calyx revealed an irregular, "moth eaten" appearance typical of tuberculosis with calcified material in and adjacent to it Urine from the right kidney was subsequently reported positive for acid fast bacilli

The patient was instructed to have the right kidney removed after the Addison's disease had been suitably managed He was discharged to the care of the referring physician who was advised to administer desoxycorticosterone 3 mg thrice weekly, sodium chloride 6 gm daily and lipo adrenal cortical extract 1 cc daily

In 6 weeks the patient returned, having gained 18 pounds of weight The pyuria persisted but the complete blood count and the blood urea and sodium chloride were normal The blood pressure was 108 70

Five days later a right nephrectomy was performed while administering adrenal cortical extract Ringer's lactate solution and sodium chloride During the operation the systolic blood pressure averaged 60 mm of mercury On the first postoperative day the blood urea, sodium, chloride and carbon dioxide combining power were normal and except for a slight drop in the sodium chloride remained normal during the next 4 days On the second postoperative day the temperature rose to 103F and remained in that vicinity thereafter Throughout the postoperative period the patient received intense adrenal cortical replacement therapy with intravenous fluids designed to maintain electrolyte balance Careful studies were made including urinary 17-ketosteroids and glucosteroids The details of these studies and the management of the patient will form the basis of a later report by *one* of us (R S) In spite of what was thought to be adequate replacement therapy and other appropriate measures including the administration of streptomycin the patient continued to have fever, developed severe asthmatic seizures and expired on the fifth day following operation Pathologic examination of the removed kidney showed findings typical of renal tuberculosis and tuberculous ureteritis The postmortem examination revealed active and chronic tuberculosis of both adrenal glands resulting in complete destruction of normal gland elements Tuberculosis of the left epididymis was also present The left kidney was found to be normal

Case 2 A 63 year old white man presented himself in April 1948, complaining of frequency of urination and nocturia every hour with initial and terminal burning present for 2 years During the 6 months preceding examination he had experienced anorexia loss of 50 pounds of weight, weakness to the extent that he was barely able to walk and increasing pigmentation of the hands and face

On physical examination the patient was found to be well developed but poorly nourished with light and dark hyperpigmentation of the skin of the face, neck, hands arms and genitalia The blood pressure was 68 48 and the peripheral pulse barely perceptible All peripheral reflexes were diminished and the motor coordination was poor The examination was otherwise negative

Laboratory studies revealed 2 plus albuminuria, 4 plus pyuria and 2 to 5 red

It has sometimes been the practice to place these patients on a free salt diet in an attempt to produce a crisis and thereby establish the diagnosis. However, this procedure is not without risk and is seldom required.

It is most important that the urologist be aware of co-existing adrenal insufficiency in a patient having renal tuberculosis because the surgical risk is so great that operation may be contraindicated or undertaken with great caution and careful planning. Greene, Walters and Rowntree[6] in 1933 described the first case of Addison's disease to survive an operation and called attention to the need for careful pre- and postoperative administration of cortical extract and salt. Kristan[7] describes the case of a service man discharged in 1943 with weakness and energy loss attributed to hypothyroidism and eczema. Two years later he was found to have renal tuberculosis and a nephrectomy was performed. Ten hours after operation the patient lapsed into a state of adrenal insufficiency which was recognized and overcome with cortical extract and sodium chloride. Such a course is more or less typical of what can happen to those patients when operated upon and more often than not the outcome is less favorable.

The following 3 cases are presented with the hope of demonstrating the problems encountered in diagnosis and the measures employed in treating renal tuberculosis complicated by Addison's disease.

CASE REPORTS

Case 1. A 31 year old white man was first seen in May 1947, complaining of frequency of urination, nocturia, burning on urination and painful enlargement of the left testicle of 4 months' duration. For about 3 months he had also experienced weakness, occasional nausea and vomiting and recurrent chills and fever. Penicillin treatment received elsewhere had afforded no relief; however, streptomycin therapy had relieved the urinary complaints. During the 8 months preceding our examination the patient had noticed increasing pigmentation of the skin and had lost 40 pounds in weight.

On physical examination the blood pressure was found to be 78/60. Hyperpigmentation of the skin was present over the neck and waist. The left epididymis was enlarged and quite hard. There was definite induration of the left seminal vesicle. The examination was otherwise negative.

The laboratory studies revealed severe pyuria and urine smears were positive for acid fast bacilli. A complete blood count was normal. The blood urea was 78 mg. per cent and the sodium chloride 462 mg. per cent.

Roentgen study of the chest revealed no abnormalities. An excretory urogram revealed calcifications in the vicinity of the upper pole of the right kidney on the initial film. The dye appeared promptly on both sides and no hydronephrosis was present. The calcifications were seen to be in the right superior minor calyx.

A diagnosis was made of Addison's disease with probable renal tuberculosis and suitable medication was instituted to combat the adrenal insufficiency before proceeding further.

[6] Greene, C. H., Walters, W. and Rowntree, L. G.: Ann. Surg. **98:** 1013, 1933.
[7] Kristan, J. J.: J. Urol., **61:** 178, 1949.

loss of appetite and severe sweating. For the past 4 months increased pigmentation of the skin had been observed and examination revealed characteristic pigmentation of skin and mucous membranes.

At this time the patient was placed on active adrenal cortical replacement therapy with pronounced improvement and was well at his last visit. This case is included in this report to indicate that Addison's disease may occur after urogenital tuberculosis has apparently been controlled by surgical means.

SUMMARY

Attention has been called to the possible co-existence of Addison's disease and renal tuberculosis and how one may mask the other.

Knowledge of the presence of adrenal insufficiency is important because such a patient represents a poor surgical risk.

Clinical symptoms and laboratory findings indicative of depressed adrenal function have been outlined.

Three cases have been presented which demonstrate the problems associated with management of such patients.

In the second case no operation has been done and thus far the patient has been controlled with replacement therapy for the Addison's disease and streptomycin for his renal tuberculosis. The first patient had recognized Addison's disease at the time the diagnosis of renal tuberculosis was established. In spite of a period of preoperative therapy for his adrenal insufficiency and vigorous postoperative treatment, he did not survive a quick, uncomplicated nephrectomy. A third case illustrates the development of Addison's disease 10 years after the removal of a tuberculous kidney.

CONCLUSIONS

From ou experience with these cases and from information obtained from the literature it seems justifiable to state that concomitant renal tuberculosis and Addison's disease mean poor tolerance to surgical procedures. Proper supportive therapy including adrenal cortical extracts and salt should be instituted before ever performing diagnostic instrumentation. Even when satisfactory response to such therapy has been observed a considerable degree of risk still remains.

ADDENDUM

Since this paper was compiled and presented much progress has been made in the treatment of adrenal insufficiency. With improved management it is even more important that Addison's disease be recognized when occurring in association with genitourinary tuberculosis.

blood cells per high powered field of urine examination. A complete blood count including red cells, white cells, hemoglobin and differential smear was normal. The blood urea was elevated to 87 mg. per cent and the potassium to 34.3 mg. per cent (8.8mEq/L). The serology was negative and the blood sugar, sodium chloride, uric acid, calcium, phosphorus and sodium were normal. The urinary 17-ketosteroids were 0.8 mg. per 24 hours (normal equals 6 to 14 mg. per 24 hours) by the fractionation method of McCullagh and Bowman.[8] A catheterized bladder urine specimen revealed Streptococcus fecalis and Staphylococcus albus organisms when cultured. The electrocardiogram was not remarkable.

An x-ray of the chest revealed no abnormalities. On excretory urography the initial film revealed multiple small calcifications over the lower pole of the left kidney and a single calcification over the upper pole. The dye was not present in either kidney in 5 minutes but appeared in the right kidney in 15 minutes and the renal pelvis appeared grossly normal. No dye appeared in the left kidney at the end of 1 hour. The cystogram revealed a bladder smaller than normal.

A diagnosis of Addison's disease was made and bilateral renal tuberculosis strongly suspected. The patient was given an initial dose of desoxycorticosterone 5 mg. and was placed on sodium chloride 2 gm. 3 times daily. Adrenal cortical extract was then given morning and afternoon every other day in 10 cc doses. On the sixth day after institution of therapy cystoscopy and left retrograde pyelography were performed. A diffuse low grade cystitis was noted with two bright red areas present on the dome. The trigone and ureteral orifices were normal. The left ureter was catheterized without meeting any obstruction, a specimen of urine was obtained and a retrograde pyelogram done. The pyelographic pattern was consistent with tuberculous infection and the urine specimen was subsequently reported positive for acid fast bacilli.

The severity of the patient's adrenal insufficiency prompted us to defer any surgical procedure and a course of streptomycin and chaulmoogra oil was instituted and was continued by the referring physician. Before discharging the patient a 375 mg. dose of desoxycorticosterone in pellet form was surgically buried in the left axilla. At the time of discharge the blood urea was 36 mg. per cent and the urinary 17-ketosteroids were 1.7 mg. per 24 hours.

Case 3. A 40 year old white man was first seen in 1939 complaining of a chronic urethral discharge which had been present for several years. There was a past history of sanatorium care for pulmonary tuberculosis from 1928 to 1932, and he had had a right epididymectomy performed for tuberculosis in 1931. Complete investigation revealed a prostatovesiculitis and a questionable deformity of the left renal pelvis, but bacteriologic study failed to reveal any tubercle bacilli in the urine. However, recheck examination on the next observation 1 year later revealed extension of the lesion in the left kidney and tubercle bacilli were demonstrated in the left kidney urine. The right kidney was negative. Nephrectomy was advised and carried out elsewhere.

The patient was not seen again until 1950 when he returned with the classical picture of Addison's disease. He had observed anorexia, progressive weakness, away rather than into the kidney substance so that involvement of the cortex is often minimal unless the cyst happens to be located in the center of the kidney. It is this centrally situated type that is more likely to be confused with cortical tumor. Most cysts are found in either the lower or upper pole. One often notices a special line of demarcation in the excretory urogram between the mass in question and the normal cortex. Tumor may infiltrate and obstruct the renal vessels and reduce function in which there is less demarcation between the mass and cortex. In tumor the density is likely to be greater than that of cyst and in the latter the outline for the psoas muscle may not be obliterated. The weight of the cyst has been known to produce other changes in the x-ray of which the most prominent are ptosis, rotation and deviation in both the longitudinal and transverse axes. ·On palpation a renal cyst is apt to be more movable, round and resilient. A solid tumor must never be overlooked and let us emphasize that we would not base a course of management from x-ray findings alone. We do contend that most large renal cysts can be suspected and correctly diagnosed and it is our object to call attention to a simple aid in diagnosis which we have used in this clinic for the past 9 years. The simple aspiration of renal cysts has no originality with us, as it has been reported by Fish, Dean and Wheeler.

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[8] McCullagh, D. R. and Bowman, W. E.: Endocrinol., 27: 525, 1940.

When renal cysts are strongly suspected from the x-ray and other findings, and with the object of conservative therapy in mind, we have resorted to a simple office procedure to confirm the diagnosis. We have simply inserted a lumbar puncture needle through the patient's back into the cyst. The technique is similar to perirenal air injection but without the danger inherent with forcing air into vascular areas. A plain x-ray first obtained in the upright position usually shows the relation of the mass in question to the lumbar vertebrae and the posterior crest of the ilium. With the patient then in the sitting position novocaine is injected toward the center of the mass and along the lateral border of the sacrospinalis muscles. This is followed by insertion of a lumbar puncture needle, usually 18 gauge. One feels a decrease in resistance to the needle as it passes through the quadratus lumborum muscle into the perirenal fat. The wall of a simple cyst is usually fibrous and the point of the needle enters with unmistakable resistance. If the needle has entered the cyst the end will go up and down on respiration. We then aspirate 30 to 50 cc fluid or allow it to escape. A similar amount of excretory contrast medium is then injected. If a diagnosis of simple cyst is then confirmed, future management can be carefully considered and this need not be necessarily surgical exploration of the cyst with excision or nephrectomy. Detailed chemical analyses of the fluid have been made but do not appear to be important. As a precaution against the remote possibility of concomitant malignant tumor the fluid is sent for study by the Papanicolaou method. The fluid is usually crystal clear or slightly yellowish. If a hemorrhagic cyst is encountered the possiblity of malignancy is 25 to 35 per cent according to the literature. We have never encountered a hemorrhagic cyst in which the implications of malignancy would obligate surgical exploration. This procedure has not inconvenienced a single patient and has been quickly and simply done in the office. In twenty odd cases it has confirmed our provisional diagnosis of simple

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THE DIFFERENTIAL DIAGNOSIS BETWEEN RENAL TUMORS AND CYSTS

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This communication deals with the differential diagnosis between cortical tumors and *large* cysts of the kidney. No attempt is made to discuss the various theories of the etiology of cystic disease of the kidney, nor are we concerned with the various classifications into so-called hemorrhagic, multilocular, hydatid, retention, polycystic disease, cystic degeneration or cyst which communicates with the pelvis or calyces. It should be clear that the type of cyst to which we refer in these recorded experiences is the so-called solitary or simple cyst. They are rather large cysts which occasionally occur in connection with the kidneys; in some instances they are bilateral. It was thought at one time that such cysts were exceedingly rare and in 1928 Colston stated that one had not been encountered at the Brady Urological Institute. As the general use of x-rays has become more commonplace, it is now realized that large, simple or serous cyst of the kidney occurs much more frequently than was formerly supposed. In the early thirties Quinby quoted Simkow as collecting 315 cases and by 1939 Fish had reported his experience in 32 cases over a ten year period.

Symptomatology and x-ray findings in renal cortical tumor are often characteristic leaving little to speculation. We are occasionally confronted with space-occupying lesions of the renal cortex in which all of the findings strongly suggest a solitary cyst. It is our belief in such instances that surgical exploration is unnecessary if it can be established that the lesion is a solitary cyst and not a solid tumor. Renal cysts rarely produce the severe constitutional symptoms of cortical tumor, such as weight loss, emaciation, anemia, fever and the other findings of malignant or metastatic neoplasms. They may mimic gastro-intestinal diseases or produce local or referred pain purely by the pull of their weight. Hematuria is not uncommon. Most renal cysts of this type are asymptomatic and have been discovered inadvertently during the course of x-ray or general physical examination.

The most important diagnostic feature is the appearance of the x-rays in which the cysts have often a distinctly different appearance than solid tumors. The mere fact that a large, circular mass is found attached to the lower pole of the kidney without evidence of metastases or constitutional symptoms alone suggests cystic disease instead of cortical renal tumor. Renal cysts are more likely to produce a circular shadow with an even contour in the x-ray film and as a rule do not result in much change in the outline of the kidney. The extent of the deformity in the calyces and pelvis depends on the position and size of the cyst. The calyceal and pelvic defect is usually crescentic and even in outline rather than irregular when an infiltration process is present. Cysts tend to grow away rather than into the kidney substance so that involvement of the cortex is often minimal unless the cyst happens to be located in the center of the kidney. It is this centrally situated type that is more likely to be confused with cortical tumor. Most cysts are found in either the lower or upper pole. One often notices a special line of demarcation in the excretory urogram between the mass in question and the normal cortex. Tumor may infiltrate and obstruct the renal vessels and reduce function in which there is less demarcation between the mass and cortex. In tumor the density is likely to be greater than that of cyst and in the latter the outline for the psoas muscle may not be obliterated. The weight of the cyst has been known to produce other changes in the x-ray of which the most prominent are ptosis, rotation and deviation in both the longitudinal and transverse axes. On palpation a renal cyst is apt to be more movable, round and resilient. A solid tumor must never be overlooked and let us emphasize that we would not base a course of management from x-ray findings alone. We do contend that most large renal cysts can be suspected and correctly diagnosed and it is our object to call attention to a simple aid in diagnosis which we have used in this clinic for the past 9 years. The simple aspiration of renal cysts has no originality with us, as it has been reported by Fish, Dean and Wheeler.

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* Deceased.

When renal cysts are strongly suspected from the x-ray and other findings, and with the object of conservative therapy in mind, we have resorted to a simple office procedure to confirm the diagnosis. We have simply inserted a lumbar puncture needle through the patient's back into the cyst. The technique is similar to perirenal air injection but without the danger inherent with forcing air into vascular areas. A plain x-ray first obtained in the upright position usually shows the relation of the mass in question to the lumbar vertebrae and the posterior crest of the ilium. With the patient then in the sitting position novocaine is injected toward the center of the mass and along the lateral border of the sacrospinalis muscles. This is followed by insertion of a lumbar puncture needle, usually 18 gauge. One feels a decrease in resistance to the needle as it passes through the quadratus lumborum muscle into the perirenal fat. The wall of a simple cyst is usually fibrous and the point of the needle enters with unmistakable resistance. If the needle has entered the cyst the end will go up and down on respiration. We then aspirate 30 to 50 cc fluid or allow it to escape. A similar amount of excretory contrast medium is then injected. If a diagnosis of simple cyst is then confirmed, future management can be carefully considered and this need not be necessarily surgical exploration of the cyst with excision or nephrectomy. Detailed chemical analyses of the fluid have been made but do not appear to be important. As a precaution against the remote possibility of concomitant malignant tumor the fluid is sent for study by the Papanicolaou method. The fluid is usually crystal clear or slightly yellowish. If a hemorrhagic cyst is encountered the possiblity of malignancy is 25 to 35 per cent according to the literature. We have never encountered a hemorrhagic cyst in which the implications of malignancy would obligate surgical exploration. This procedure has not inconvenienced a single patient and has been quickly and simply done in the office. In twenty odd cases it has confirmed our provisional diagnosis of simple cyst and has proved of considerable value in the management. The followin cases selected from our service serve to illustrate the practical value of thi procedure.

CASE REPORTS

Case 1. C. C. R., University of Virginia No. 135519, a 65 year old man, was admitted with the diagnosis of lower right ureteral calculus. We were surprised to note on excretory urography that there was a large mass attached to the outer and lower pole of the left kidney. The mass had all the x-ray characteristics (fig. 1, *A*) of a simple cyst of the lower pole, which was producing little pressure on the cortex. Aspiration of clear fluid and the injection of opaque material into the mass (fig. 1, *B*) confirmed the diagnosis of a simple, benign and asymptomatic cyst in the lower pole of this kidney. The patient was discharged without exploration and he has been followed for almost 3 years without the development of any symptoms or evidence of change in the size of the mass.

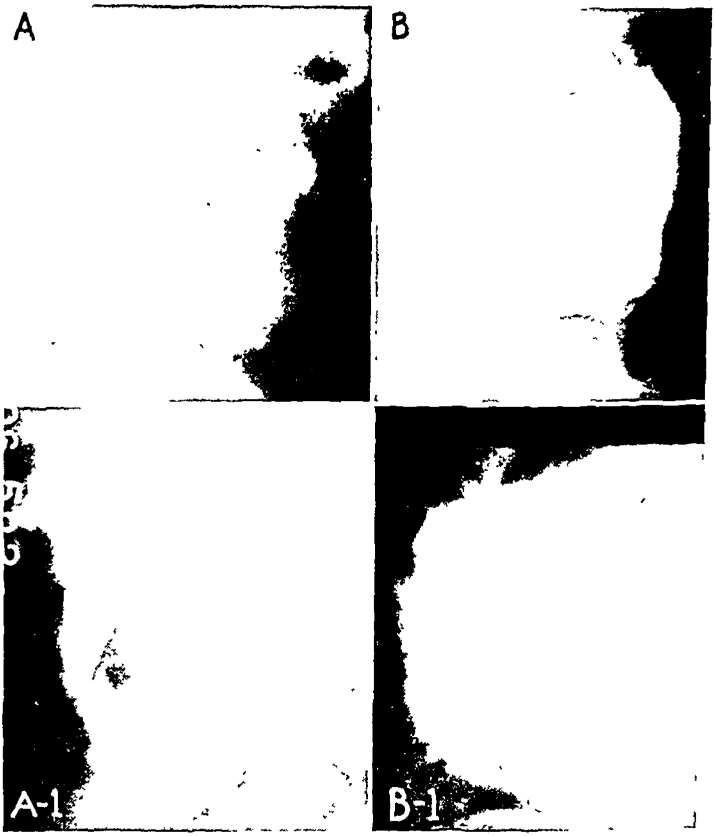

FIG. 1. *A*, pyelogram in 65 year old man with a circular shadow involving lower pole of left kidney. *B*, the same mass after withdrawal of clear fluid and injection of excretory contrast medium. It is unmistakably a cyst of lower pole.

A-1, right regrograde pyelogram in 79 year old man with hematuria. X-ray showed a circular soft tissue shadow producing marked displacement and deformity of renal pelvis. Because mass had appearance of cyst rather than solid tumor, injection of opaque medium was done. *B-1*, shows mass to be cystic after injection.

Case 2. J. H. W., University of Virginia No. 158224, a 79 year old man, was admitted because of painless hematuria coming from the right kidney. Retrograde pyelogram (fig. 1, *A-1*) showed the right kidney rotated outward by the pressure of a large mass which was located immediately anterior and somewhat on the mesial side of the kidney. It had an even outline and had more the appearance of a cyst than a malignant tumor. We simply inserted a needle through the back and obtained clear fluid. The following renal cystogram as shown in figure 1, *B-1* resulted after the injection of contrast medium. Exploration of the kidney in a 79 year old man facing other surgery was unnecessary.

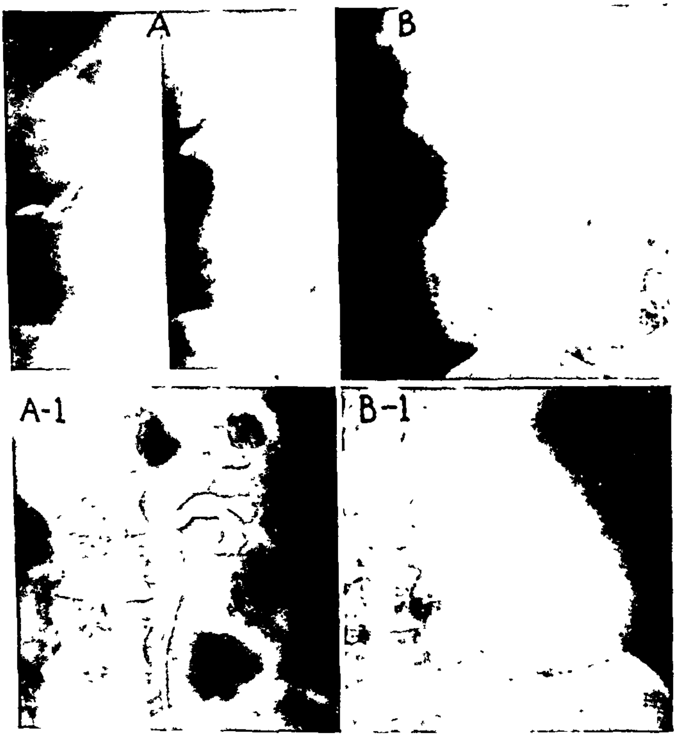

FIG. 2. *A*, retrograde pyelogram in 60 year old man who had no symptoms related to urinary tract Soft tissue shadows showed two circular masses of low density involving upper and lower poles of kidneys. *B*, confirms the nature of the masses after injection of contrast medium. It is apparent that two large single cysts involve poles of the right kidney.

A-1, normal pyelogram in 46 year old woman who complained of some discomfort in left abdomen X-ray revealed circular mass attached to lower pole of kidney that did not produce any cortical atrophy or defect in pyelogram. *B-1*, reveals mass to be a simple solitary cyst of kidney.

Case 3. N. B. J., University of Virginia No. 248089, was a 60 year old dentist who was having a gallbladder series done at home because of epigastric pain. It was noted that a marked enlargement of the right kidney was present. Excretory urograms revealed a pelvis compressed between cortical masses involving the upper and lower poles. Retrograde pyelograms confirmed this finding (fig. 2, *A*). The patient suspected that he had a malignant tumor, made his will and closed out his practice. From the x-ray the most likely diagnosi were two large solitary cysts originating from either pole of the right kidney Figure 2, *B* after injection according to the above technique shows that thi diagnosis is confirmed. The patient was extremely happy over the turn of event and has resumed his practice with a far different mental outlook. Further studies revealed that the epigastric pain resulted from advanced coronary disease and with the unpromising prognosis in his cardiac condition, we did not recommend surgery.

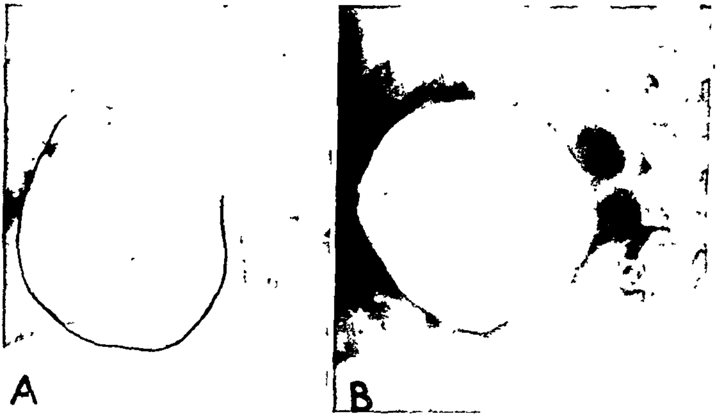

FIG. 3. *A*, retrograde pyelogram in a 44 year old woman in whom her physician palpated an abdominal mass. Pyelograms show a normal kidney with evidence of a slight pressure defect and deformity of calyx on that side. Outline of mass as indicated by x-ray, (*A*), was roughly circular. Injection a few minutes later, (*B*), after aspiration and injection revealed a single solitary cyst of that kidney.

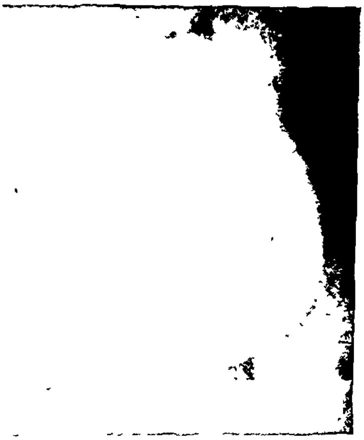

FIG. 4. Injected "renal cystogram" in 75 year old woman again in whom a mass was discovered on general examination. Excretory urograms showed an essentially normal kidney with a circular mass attached either to anterior or posterior surface of kidney. Aspiration and injection with contrast medium revealed this to be a cyst.

Case 4. P. S. E., University of Virginia *No.* 229821, a 46 year old nurse's aide complained of discomfort in her left abdomen. The pyelogram, as shown in fig. 2, *A-1*, was essentially normal but a circular mass attached to the lower pole of the kidney could be seen in the x-ray. It was obvious after aspiration and injection that a simple cyst was present (fig. 2, *B-1*.) Unlike the previous case, the cyst grew away from the kidney without producing atrophy of the cortex or any pressure defect on the calyceal or pelvic systems.

Case 5. C. H. S., University of Virginia No. 4133, was a 44 year old woman in whom her physician palpated a mass attached to the lower pole of the kidney.

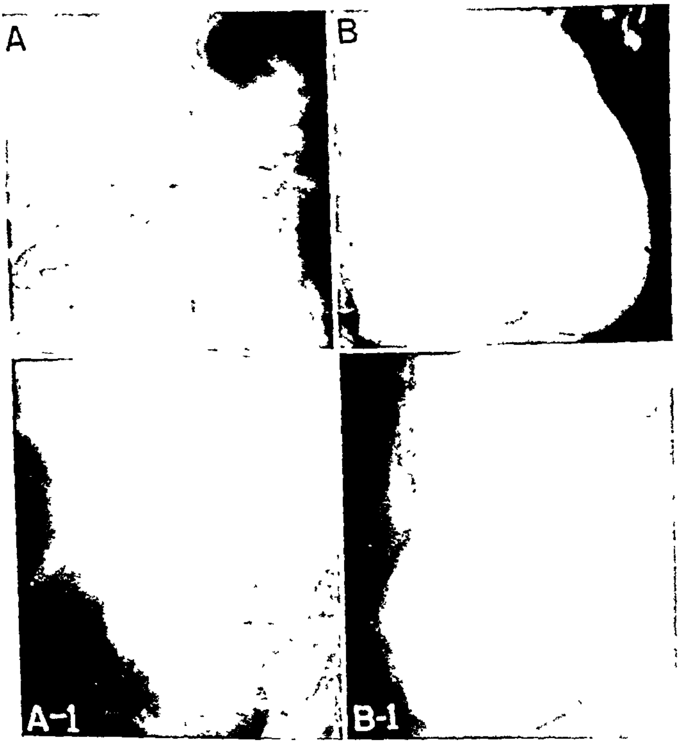

Fig. 5 *A*. pyelogram from case of 48 year old woman without symptoms showing circular shadow attached to left kidney and moderate filling defect of calyceal system. *B*, after aspiration and injection of contrast medium confirms diagnosis of simple benign cyst. Clear fluid was obtained from which cultures were sterile and cell block studies were negative.

A-1. excretory urogram from 70 year old physician who discovered a smooth mass in upper abdomen Pyelograms were indeterminate but an oval mass attached to kidney was visible *B-1*. following aspiration and injection of contrast medium confirms diagnosis of benign solitary cyst. Cultures of clear fluid were negative and cell block studies showed no cellular content.

Figure 3. *A* shows the retrograde pyelogram with the outline of the circular mass drawn roughly in ink. The simple injection in the office confirmed the diagnosis. (fig. 3, *B*) and as no symptoms were present operation was not recommended.

Case 6. R. M. B., University of Virginia No. 1840. A circular mass was palpated in the region of the left kidney in a 75 year old woman during general physical examination. Excretory urograms were essentially normal. Aspiration and injection revealed the mass to be a cyst originating from the lower pole of the kidney (fig. 4).

Case 7. W. H., No. 55039, was a 48 year old colored housewife who gave a history of cholecystectomy 11 years prior to present admission at which time the surgeon noted a solitary cyst of the left kidney. No symptoms were referable to the urinary tract, and she was referred to the urological department because of a small palpable mass discovered in the left upper abdomen in another department. Urological examination revealed a normal right upper urinary tract but with a filling defect involving the calyces on the left (fig. 5, *A*). The outline of a mass associated with that of the kidney was visible. The mass was aspirated and crystal clear fluid was obtained. Culture and cell block studies of this fluid were negative. Figure 5, *B*, after aspiration and injection of contrast medium, confirmed the cystic nature of the tumor. There has been negligible increase in size of the cyst in 11 years and practically no reduction in kidney function. Operation was considered superfluous.

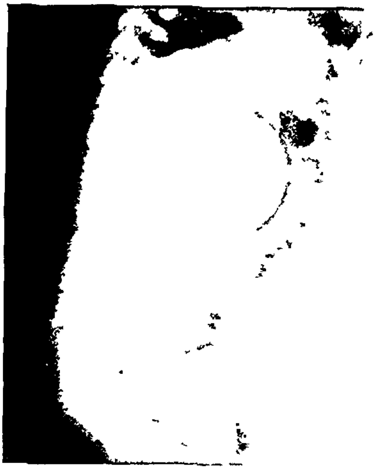

FIG. 6 Injected multilocular hydronephrosis in a 1 day old baby boy. Mass was extremely large, filling left side of abdomen, but on palpation it seemed cystic. Correct diagnosis was possible immediately without anesthesia and cystoscopy. Operation could then be more intelligently planned.

Case 8. J. M. M., University of Virginia No. 290939, was a 70 year old physician admitted for evaluation of symptoms of early congestive cardiac decompensation. A routine abdominal x-ray revealed a large oval mass approximately 20 by 14 cm. in the right upper quadrant. An excretory urogram made with diodrast showed a normal pyelo-ureterogram on the left side but an indeterminate picture on the right (fig. 5, *A-1*). The mass was palpable, smooth in outline and fixed to the kidney. It moved with respiration. Aspiration of the mass yielded clear but straw colored fluid. Culture was sterile and cell block studies showed no cellular content. Injection of contrast medium confirmed the diagnosis of benign solitary cyst of the right kidney for which operation was not indicated.

It is hoped that these selected instances serve to illustrate the value of this simple procedure in assisting with the diagnosis of renal mass when simple cystic disease is strongly suspected. The procedure in our hands has been entirely harmless, essentially painless, and there is no more risk involved than the injection of procaine or excretory contrast medium.

The following instance in a young infant serves to illustrate the use of this procedure in cases of suspected hydronephrosis in which excretory or retrograde pyelograms are uninformative or undesirable.

Case 9. D. E. F., University of Virginia No. 278464, was a day old baby referred because of a palpable mass in the left abdomen. An excretory urogram showed a normal kidney on the right but absence of dye on the left. On palpation the mass seemed to be resilient and had the sensation of being cystic in nature rather than a solid tumor. Because the latter indicated hydronephrosis or cyst of the kidney, it was decided to confirm the diagnosis by this method and not subject the tiny infant to cystoscopy. It was very simple to insert a needle just lateral to the sacrospinalis and enter the cystic mass. We encountered yellow fluid which had the appearance of dilute urine. The injection of opaque material (fig. 6) revealed conclusively that we were dealing with a case of large congenital hydronephrosis. The anxious parents were reassured and 2 days later the hydronephrotic sac was deflated through a small incision in the lumbar area and easily removed without difficulty.

DISCUSSION

It is generally accepted and so recorded that surgical exploration for all space-occupying lesions of the kidney is an immediate necessity. It is our belief to the contrary that exploration is neither desirable nor necessary in most instances of so-called solitary cysts of the kidney when the diagnosis can be confirmed. Braasch so stated in 1935 that exploration was definitely indicated in all cases but admitted that if large cysts were inadvertently discovered by surgeons in patients over 50 years of age that they had best be left alone. Most cysts tend to grow away from the kidney and only in rare cases is excision indicated for the preservation of functioning renal tissue. It is also our impression that most cysts are self-limiting in size, although an occasional one of giant proportions has been reported. We have encountered a number in the older age group which have evidently been present many years with little damage to the cortex or tendency to increase in size.

When symptoms of pain, discomfort, excessive hematuria or evidence of progressive cortical damage are present, then excision is in order. When excretory urography tells us that a relatively small amount of cortex has been rendered nonfunctioning by pressure and when there are no symptoms, it is our conclusion that conservative management is indicated. As a matter of fact, Archie Dean reported excellent results in 15 cases treated by simple aspiration of the contents in the manner reported here. In 1939, Fish reported 2 cases cured by aspiration and the injection of a 50 per cent solution of dextrose. In other cases in which he injected air there was gradual refilling. Operations for the removal of cysts from the kidney are not always simple and the necessary suturing to control bleeding may inactivate more cortex than would the presence of the cyst had it been allowed to remain. Large cysts of the kidney do not easily shell out as the walls may be lined in part by low cuboidal cells and in other areas by fibrous tissue which is not readily separated from the kidney.

It is expected that the controversial points about this procedure will be resolved into two questions. The first concerns the advisability of inserting a needle into a malignant tumor and possibly depositing cells along the tract as the needle is withdrawn. It is conceivable a curable condition might thus be converted into an incurable one. We do not advocate inserting a needle into malignant tumors, although Dean once reported 135 aspiration biopsies of malignant renal tumors and in his opinion there was never any "evidence of harm." Many urologists have emphasized that it is practically impossible to differentiate cysts from tumors. It is difficult for us to understand such statements. This may be true from a single x-ray but from our study of a series of x-rays, both excretory and retrograde, and correlating these with the appearance of the patient, palpation of the mass and the history, we believe one can predict the possibility of cyst with considerable accuracy. The proof of this is that in the last 9 years we have been uniformly correct in our appraisal of cyst. We have suspected solitary renal cyst in some twenty odd cases and in every instance we have tapped a cyst in which clear fluid has been withdrawn and in which there has never been any question of malignancy. In only one instance have we inserted a needle into a malignant tumor and this in a patient who refused operation. In this case we predicted tumor would be present because changes in the upper calyces indicated infiltration in the opposite pole of the kidney.

The second controversial point, i.e. overlooking a malignant tumor, is a highly important one. There are a few references in the literature concerning the association of malignant cortical tumors and cysts of the kidney. A review of these reported cases convinced us that they do not bear critical analysis as data on such association. In the type of case to which we refer the fluid is clear and the injected "renal cystogram" shows a generally smooth outline without any evidence of solid tumor. One would certainly not confuse the reported cases of solid tumor within which there has been secondary cystic degeneration. For an example, in the quoted case of Ezickson and Greene the fluid was reported as muddy and the published photograph showed the wall of the cyst cavity lined with irregular papillary tumor. There is certainly no relationship between such a cystic change in a malignant tumor and the thin, clear wall cyst upon which we base our experience.

There have been a few chance associations between cysts and solid tumors. Colston once operated for a papillary cyst adenoma involving the upper pole in the renal pelvis in which there was no mistaking the preoperative diagnosis. At operation there was an additional small cyst attached to the lower pole of left kidney which bore no relationship to the papillary tumor in the upper pole. A similar situation has been reported by Greenberg, et al. We must always think of malignancy when dealing with the genito-urinary tract, but we believe that the association with cyst is purely one of coincidence and this chance occurrence is not enough to merit surgical exploration as the only recommended therapy in every case of cyst. We further believe that the injection of contrast medium should lead one to suspect the presence of a defect in the wall if a solid tumor was also present. Papanicolaou stains should prove helpful when cells are present in the aspirated fluid. If one aspirates hemorrhagic material exploration is in order.

It is our considered judgment that the procedure which we have followed in the diagnosis and management of solitary cyst of the kidney has proved to be more conservative and sensible than routine exploration. Let us emphasize that we have selected our cases with care and have used this procedure only when we have strongly suspected cysts to be present. In some instances in which the cyst was small and situated in the center or hilum region of the kidney, we have recommended and carried out exploration. Though the contour of the mass suggested cyst, we did not wish to chance the insertion of a needle into such a centrally located solid tumor. When cysts are larger and situated in either pole we have felt more sure of ourselves and have not hesitated to use the suggested procedure with uniform success.

CONCLUSIONS

Contrary to most opinion large simple cyst of the kidney can be suspected from the appearance of the x-rays, history and general findings.

In most cases of large renal cyst, surgical exploration is unnecessary and undesirable.

The diagnosis is easily confirmed by the x-ray appearance of "renal cystograms." These are achieved by aspiration through the back and the injection of excretory contrast medium.

As an office procedure it is painless, harmless and logical.

It is useful in cases of hydronephrosis in infants and adults in selected instances in which cystoscopy is unsuccessful or undesirable.

REFERENCES

COLSTON, J. A. C.: Solitary cyst and papillary cystadenoma occurring simultaneously in one kidney. J. Urol., **19**: 285–290, 1928.

DEAN, A. L.: Treatment of solitary cyst of the kidney by aspiration. Trans. Am. Assn. of Genito-Urin. Surg., **32**: 91–95, 1939.

EZICKSON, W. J. AND GREENE, L. B.: Solitary cyst of the kidney with adenocarcinoma in the walls of the cyst. J. Urol., **38**: 153–159, 1937.

FISH, G. W.: Large solitary serous cysts of the kidney. J.A.M.A., **112**: 514, 1939.

GREENBERG, B. E., BRODNY, M. L. AND ROBINS, S. A.: Solitary cysts of the kidney. Am. J. Surg., **23**: 271–283, 1934.

KUTZMAN, N. AND SAUER, H. R.: A consideration of the problems presented by unilateral cystic kidney disease. J. Urol., **63**: 34–47, 1950.

QUINBY, W. C. and BRIGHT, E. F.: Solitary renal cysts; their symptoms when situated at the upper pole of the right kidney. J. Urol., **33**: 201–214, 1935.

RITTER, J. S.: Mesothelial type of malignant hypernephroma within a solitary cyst of the kidney. Am. J. Surg., **8**: 1089–1091, 1930.

WHEELER, B. C.: Use of aspirating needle in diagnosis of solitary renal cyst. New Eng. J. Med., **226**: 55–57, 1942.

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MALAKOPLAKIA OF THE BLADDER

DANIEL R. HIGBEE AND THOMAS E. KILFOYLE

Malakoplakia (derived from the Greek word "malakos" meaning soft) is a lesion of the genito-urinary tract first described in detail by Von Hansemann in 1903, although Michaelis and Gutmann in 1902 had observed 2 cases. Since that time sporadic cases have appeared in the literature, the most recent being 2 cases presented by Cristol and Broders.

The disease is not one of the bladder alone. In addition, it may involve the ureters, kidney pelvis, and even the kidney parenchyma as described by McDonald and Sewell.

The lesion may present itself to the cystoscopist in many bizarre patterns. The plaques may be single or multiple, varying in size from a pinhead to large coalescent masses which may extend 1–2 cm. into the bladder lumen. They are most often described as soft greyish-brown elevations, the centers of which may be umbilicated with a surrounding zone of hyperemia. Their distribution in the bladder is variable.

Most authors are in full agreement as to the microscopic appearance of malakoplakia. The lesion is one of the submucosa with the overlying bladder epithelium usually intact, although in some cases it may be partially destroyed. The characteristic cell is a large, round or oval but sometimes polygonal cell usually mononucleated with a well-defined cell membrane. The cytoplasm is most often granular and highly refractile. Often the nucleus is absent or its presence masked by the Michaelis-Gutmann bodies. The latter vary in size and may be found within the cells or between them. They have a strong affinity for hematoxylin which stains them a purple color and many of them have concentric laminations suggestive of corpora amylacea. In general, they are homogeneous, highly refractile, and contain iron and calcium. Scattered throughout the lesion, especially near the periphery, are many polymorphonuclear leukocytes. In addition, one may find cells of the lymphocytic series and comparatively unaltered red corpuscles both in and between the large mononucleated cells.

Malakoplakia may occur in both sexes at any age, although it is most common in women over 30 years. The presenting history is usually one of intermittent attacks of cystitis.

The diagnosis is confirmed by microscopic examination although it may be suspected by finding the typical lesions at cystoscopy.

The treatment of choice in most cases is fulguration although if the lesions are accessible, they may be excised. Autogenous vaccines and potassium iodide applied locally have also been used. However, thus far too few cases have been reported to permit any standardization of treatment.

The etiology is unknown. Tuberculosis has been suggested as a possible cause

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Read at annual meeting, South Central Section, American Urological Association, Tulsa, Okla. September 27, 1950.

although numerous cases have been reported in patients who have shown no evidence of that disease. McDonald and Sewell advanced the theory that the lesions may be suprarenal cell rests since the appearance and distribution of the malakoplakia cell so closely resemble that of the suprarenal. They postulated that these cell rests may be stimulated to activity by some specific organism, possibly E. coli which are found so commonly in patients with malakoplakia. Organisms resembling E. coli have been described as possible etiologic factors although it seems difficult to believe how this organism, such a common offender in urinary tract infections, could per se be the sole cause of such a rare condition. Dickson, Gray, and Kidd have expressed the opinion that the inclusion bodies may be mycotic parasites but Rudnick and Ragins were unable to find a similar organism in their case. Redewill has reported 1 case of generalized sarcoidosis that was found to have malakoplakia. He points out the histologic similarity of the two conditions.

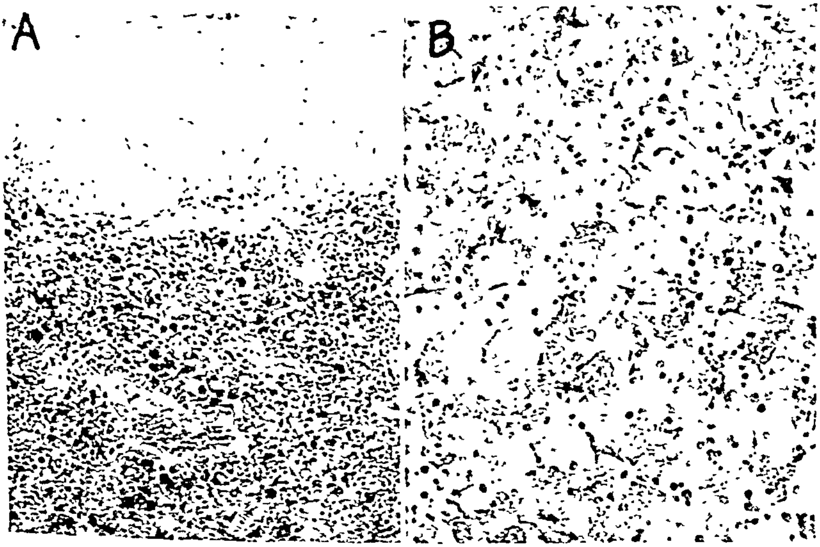

FIG. 1. *A*, showing large polyhedral cells with focal deposits of calcium. Note normal bladder epithelium. H and E stain. *B*, section stained with Sudan III showing lipoid deposits with large monocytic cells.

CASE REPORT

A 47 year old white married woman entered the hospital February 9, 1950, with a history of recurrent attacks of hematuria of 3 years' duration. A nephropexy had been done 11 years previously. Cystoscopy revealed a smooth, semipedunculated mass protruding from a pedicle on the floor of the bladder neck and extending about 1–2 cm. into the lumen. This mass was greyish-brown in color and wider at its apex than at its base. Retrograde pyelograms were negative.

At operation, this mass was friable enough to be partially removed by transurethral excision without current. However, the base was firmer and required cutting current for removal.

The following is a microscopic description of the lesion (fig. 1): "Sections show *the bladder mucosa elevated in coarse bluntly rounded projections formed by* accumulation of numbers of large monocytes and of leukocytes of various types in the lamina propria. There are focal deposits of calcium salts, spheroidal and laminated, measuring up to 20 microns in diameter. They are located within the cytoplasm of monocytes. These cells are granular, with small compact nuclei. They contain ingested lipoid, as shown by frozen sections stained with Sudan III, and also erythrocytes and leukocyte nuclei. A network of capillaries extends throughout the lamina propria, and congested large vessels are present. The epithelium is of the transitional type and is intact with hydropic changes in some fields. The lesion is not malignant."

SUMMARY

A case of malakoplakia of the urinary bladder is reported and a brief review of the literature is given.

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REFERENCES

CHISHOLM, A. E. AND TUDHOPE, G. R.: Malakoplakia of the urinary bladder. Endinburgh M. J., **41**: 626–629, 1934.

CRISTOL, D. S. AND BRODERS, A. C.: Malacoplakia of the bladder. J. Urol., **55**: 260–266, 1946.

DICKSON, W. E. C., GRAY, A. C. E. AND KIDD, F.: Malacoplakia vesicae; *an investigation* of certain mycotic infections of genito-urinary tract. Urol & Cutan. Rev., **31**: 611–621, 1927.

FOLSOM, A. I.: Malakoplakia of the bladder. J.A.M.A., **73**: 1112–1114, 1919.

VON HANSEMANN: Uber Malakoplakie Der Harnblase. Virchows Arch. f. path. Anat., **173**: 302–308, 1903.

McDONALD, S. AND SEWELL, W. T.: Malakoplakia of the bladder and kidneys. J. Path. & Bact., **18**: 306–318, 1914.

MICHAELIS, L. AND GUTMANN, C.: Ueber Einschlusse in Blasentumoren. Ztschr. f. klin. Med., **47**: 208–215, 1902.

REDEWILL, F. H.: Malakoplakia of the urinary bladder and generalized sarcoidosis, striking similarity of their pathology, etiology, gross appearance and methods of treatment. J. Urol., **49**: 401–407, 1943.

RUDNICK, D. F. AND RAGINS, A. B.: Malakoplakia of the bladder; case report. J. Urol., **42**: 108–117, 1939.

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PREVENTION OF URINARY INCONTINENCE FOLLOWING RADICAL PROSTATECTOMY: A PRELIMINARY REPORT

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Prevention of urinary incontinence following radical perineal prostatectomy is a problem which has not yet been satisfactorily solved. Of 84 cases followed by Twinem and Davalos,[1] eighteen (21.6 per cent) had partial or total incontinence. Jewett[2] reported that, in spite of the adoption of Vest's method of urethro-vesical anastomosis, 12 per cent of 100 patients with radical perineal prostatectomy remained permanently incontinent. Of 14 patients reported by Higbee[3] 7 were partially or totally incontinent.

Young[4] ascribed the frequency of urinary incontinence following radical prostatectomy to injury of the external sphincter or its nerve supply. Accordingly, retropubic radical prostatectomy, which leaves the pelvic floor undisturbed, should not be followed by incontinence. This seems to be borne out by the reports which thus far have been published on the retropubic operation. Millin[5] wrote that full urinary continence should always be obtained provided, that damage to the compressor urethrae is scrupulously avoided. Memmelaar[6] reported 30 cases of which 50 per cent had postoperative stress incontinence lasting 1 to 2 weeks. Lich, Grant and Maurer[7] reported stress incontinence lasting 1 to 2 days following catheter removal in 3 radical retropubic operations. These reports seem to indicate that urinary incontinence is not to be feared following radical retropubic prostatectomy. However, my personal experience has been different. To date I have performed 8 radical retropubic operations. The first 4 were operated on according to the usual technique as first described by Millin.

CASE ABSTRACTS

Case 1. D. C., aged 55. Catheter removed 30 days after operation; patient totally incontinent. Urinary control improved over a period of several months. At present, 19 months after the operation, he is continent while lying down and can start and stop the urinary stream with perfect control in the upright position. However, as soon as he fails to concentrate on contracting his sphincter he loses his urine. This man evidently has perfect sphincter control, but for practical purposes he is incontinent.

Case 2. L. J., aged 63. Catheter removed 18 days after operation; patient incontinent except for some measure of control lying down. Urinary control

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[1] Twinem, F. P. and Davalos, A.: J. Urol., 61: 575, 1949.

[2] Jewett, H. J.: J. Urol., 61: 277, 1949.

[3] Higbee, D. R.: J. A. M. A., 139: 141, 1949.

[4] Young, H. H.: J. Urol., 53: 188, 1945.

[5] Millin, T.: Retropubic Urinary Surgery. Baltimore: Williams & Wilkins, 1947, p. 156.

[6] Memmelaar, J.: J. Urol., 62: 340, 1949.

[7] Lich, R., Grant, O. and Maurer, J. E.: J. Urol., 61: 930, 1949.

began to improve 10 weeks after the operation. At present, 13 months after the operation, he can start and stop urination with perfect control and walk for one half hour without losing urine. However, he still wears pads or uses a Cunningham clamp.

Case 3. A. G. died of massive pulmonary embolism before the catheter could be removed, and therefore must be excluded from this series.

Case 4. L. M., aged 50. Catheter removed 23 days after operation; patient totally incontinent. At present, 7 months after the operation, he has regained a fair degree of urinary control. Starting and stopping is done perfectly, but when his bladder fills up to 100 cc or more he loses some urine. He uses 2 to 3 pads daily and on some occasions, such as going to the movies, he uses a Cunningham clamp.

DISCUSSION

These cases demonstrate that a perfectly functioning external sphincter does not necessarily insure perfect urinary control and suggests that our present concept of the sphincter mechanism should be revised. Since removal of the internal sphincter does not ordinarily produce incontinence, we have accepted the belief that only the external sphincter is indispensable for normal urinary control. This, however, does not agree with our daily experience. Cases have been reported in which perfect urinary control persisted in spite of complete destruction of the external sphincter. Occasionally incontinence follows transurethral resection of the prostate in spite of careful technique, especially if some tissue is removed below the verumontanum. Simple perineal prostatectomy is followed by incontinence in a certain percentage of cases in spite of meticulous avoidance of the external sphincter. Much of our difficulty in understanding the sphincter mechanism is due to the idea that urinary continence is primarily achieved by constant, voluntary contraction of the external sphincter. In reality this muscle does no more than contribute, by its inherent tonus, to the resistance of the urethra.[8] It contracts actively only if a desire to void must be suppressed. Continence is not achieved by active sphincteric contraction, but by the resistance of the urethra to the intravesical pressure. If the urethral resistance is diminished below a certain point, incontinence will result; its severity depending upon the degree of decrease of urethral resistance.

For a thorough understanding of urinary incontinence a brief discussion of the physiology of micturition will be helpful. We have accepted that urination is initiated by a contraction of the detrusor which reflexly relaxes the urethral sphincters. Although this is true under experimental conditions, it cannot explain how urination can be voluntarily started when the bladder contains only a small amount of urine, since neither the detrusor nor the internal sphincter is subject to voluntary influence. Hence one must conclude that, in the inactive stage, the urethra offers a resistance which normally cannot be overcome by an increase in the intravesical pressure. Before the bladder can empty, the urethral resistance must be decreased and this decrease is under voluntary control.

[8] Hock, E.: J. Urol., 57: 1069, 1947.

Permanent loss of urethral resistance will produce incontinence and, conversely, permanent inability to diminish this resistance will produce urinary retention. The nature of this resistance was first demonstrated by Stobbaerts[9] in a moving picture of an urethrocystogram taken during the act of micturition. Recently Muellner and Fleischner[10] have described this mechanism in detail. They found that the opening of the urethra usually preceded the detrusor contraction and was always accompanied by a lowering of the bladder base. This lowering of the bladder base is accomplished mainly by active relaxation of the pelvic floor and aided by an increase of the intra-abdominal pressure. Since the anterior urethral wall is fixed, lowering of the bladder base separates the posterior from the anterior wall resulting in a decrease of the urethral resistance. Closure of the urethra is achieved by the return of normal tonus of the pelvic floor muscles or by their contraction, especially the pubococcygeal muscles. This mechanism indicates that at least part of the urethral resistance is due to anteroposterior compression between the pubic bones and the pelvic floor rather than to circular contraction of the sphincters. Consequently, any process which permanently separates the anterior and posterior walls of the prostatic urethra or otherwise eliminates the prostatic urethra will cause incontinence if the tonus of the external sphincter is insufficient to withstand the intravesical pressure. Incontinence following transurethral resection of prostatic tissue below the verumontanum, which has commonly been attributed to a damaged external sphincter, can be better explained by loss of urethral resistance in the critical, inframontane area. Incontinence following simple, perineal enucleation of the prostate in spite of preservation of the external sphincter is based on the same principle, namely loss of critical urethral resistance. Incision of the membranous urethra, trauma to the urethra and pelvic floor and infection may cause a dilatation or even sacculation of the inframontane segment. The foregoing discussion suggests that, regardless of the approach to the gland, a high incidence of urinary incontinence should be expected following total prostatectomy.

A logical procedure for the prevention or cure of incontinence following total prostatectomy is one that restores adequate urethral resistance in the critical area by providing a support for the posterior aspect of the urethrovesical anastomosis. A fascial sling suspension seems to be best suited for this purpose. In the retropubic operation a Millin suspension can be employed. The perineal operation can be combined with a procedure similar to the Stoeckel, Goebel, Frangenheim operation for incontinence in the female. I have used a simplified Millin type procedure in combination with radical retropubic prostatectomy in four cases.

TECHNIQUE

Radical prostatectomy is performed according to the Millin technique through a midline incision above the symphysis pubis. A vertical, fascial strip is formed from the rectus sheath, its upper, free end pulled through the tunnel behind the urethro-vesical anastomosis and, after proper elevation of the anastomosis, sutured to the contralateral rectus sheath (fig. 1).

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[9] Stobbaerts, F.: Transactions. 6th International Congress of Urology, Paris: Doin et Co., 1937, vol. 2, p. 325.

[10] Muellner, S. R. and Fleischner, F. G.: J. Urol., **61:** 233, 1949.

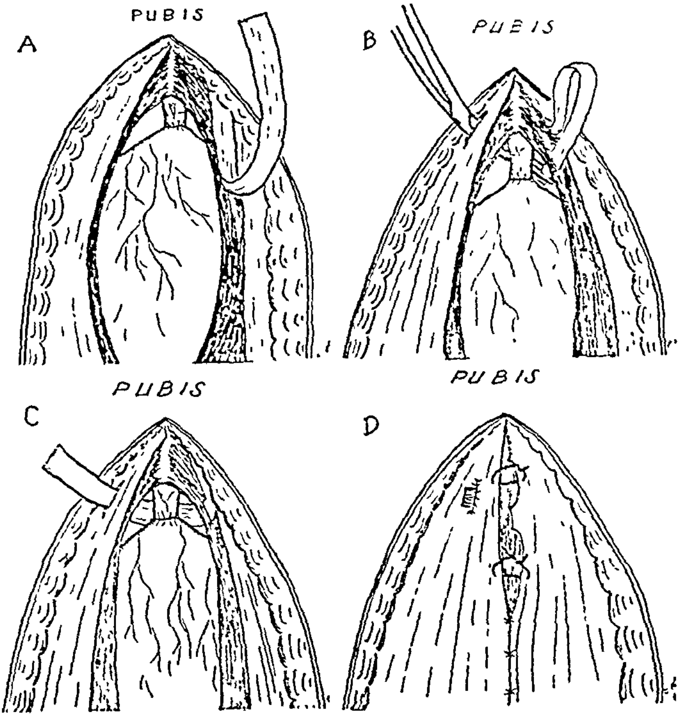

FIG. 1

CASE ABSTRACTS

Case 5. W. Z., aged 50, underwent radical retropubic prostatectomy with fascial sling operation. The catheter was removed 13 days after the operation and the patient had almost perfect urinary control the same day. He did not return for follow up treatments and was seen 4 months later with a stricture at the urethrovesical junction, urinary infection and incontinence. After dilatation of the stricture he regained urinary control.

Case 6. R. D. B., aged 51, underwent radical retropubic prostatectomy with fascial sling operation. The catheter was removed on the twelfth postoperative day. Urinary control was fairly good the same day, perfect the following day. Two days later he complained of difficulty starting to urinate. He still has some difficulty starting. Repeated examinations showed no residual urine.

Case 7. J. B., aged 51, underwent radical retropubic prostatectomy with fascial sling operation. The catheter was removed on the thirteenth postoperative day. Urinary control was perfect. Twenty-six days after the operation he had an acute urinary retention which required catheterization. The patient continued to complain of slowness of the stream and later had several episodes of urinary retention. Four months after the radical operation 1 gm. tissue was removed by transurethral resection from the bladder neck region. Since then the patient has had no further difficulty.

Case 8. S. O., aged 55, had radical retropubic prostatectomy with fascial sling operation. Catheter was removed on the seventeenth postoperative day. He had good urinary control while lying down or sitting, but was completely incontinent when standing. He regained perfect urinary control on the thirty-fifth postoperative day.

SUMMARY

Normal urinary control is produced by the resistance of the urethra to the intravesical pressure.

This urethral resistance is caused by the tonus of the urethra, its sphincters and supportive structures and not by active sphincteric contraction.

Urinary incontinence results from a substantial loss of the urethral resistance.

After total prostatectomy an intact external sphincter may be inadequate to insure normal, urinary control.

Urinary incontinence following radical prostatectomy can be prevented by using a fascial sling to elvate the urethrovesical anastomosis.

The technique of a fascial sling operation as practised in combination with radical retropubic prostatectomy has been described.

The status of urinary control of three patients following radical retropubic prostatectomy alone and of four patients following radical retropubic prostatectomy combined with a fascial sling operation has been reported.

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SPONTANEOUS ACTIVITY OF THE DETRUSOR MUSCLE IN THE CAT

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Spontaneous contractions of the urinary bladder in the intact animal have been observed by many investigators, among them Stewart (1900), who reported that automatic movements are generally present and show at times both simple and compound rhythms. He observed that simple rhythms are not always regular. He also reported that the compound rhythms consist of two or more regular or irregular rhythms and that they are due to contractions at different rates in two or more areas of the viscus. These and other pertinent reports in the subsequent literature are based either upon interpretations of the kymographic records of the total bladder responses or were determined by direct observation. Since these procedures do not provide objective data on the comparative activity of various specific regions of the muscle, an attempt has been made in the present experiment to obtain records of the motor activity taking place simultaneously in several regions of the intact viscus. From the data we have sought answers to the following questions: 1) Do all regions of the viscus exhibit spontaneous activity; and if so, are all regions equally active? 2) Do observed contractions begin in unison, are they unrelated, or is there an orderly wave of activity having any relationship to the long axis of the organ? 3) Is the activity of the muscle during micturition peristaltic or in unison? Is there an observable node of activity? 4) To what extent is the observed pattern of muscular activity altered by changes in the volume of the bladder and variations in pressure?

METHODS

Under light nembutal anesthesia the urinary bladder of the cat was exposed and on it were placed small squares of black adhesive paper each bearing a central spot of white drawing ink. The paper squares were arranged so as to divide the exposed surface of the bladder into quadrants (designated A, B, C and D) and twelve segments (fig. 4, no. 1). By means of a Ciné-kodak Special 16 mm. camera, mounted above the bladder, photographs were taken at one second intervals during each period of observation. Subsequently, by projecting the film on to suitable paper, measurements were made of the activity taking place in each segment. In addition, a kymograph record was kept of the total bladder response. In the present experiment the bladder of a single cat was observed during a series of seven periods. The intravesical pressure was held constant during a given period of observation but was varied from one period to the next. An eighth observation, using variable pressure, was made from a different animal. Details of these procedures have been described previously (Hegre and Ingersoll, 1949).

RESULTS

Observation No. 1 (fig. 1) was recorded from a slightly distended bladder in which the pressure was held constant at 4 cm. of water. While there was spon-

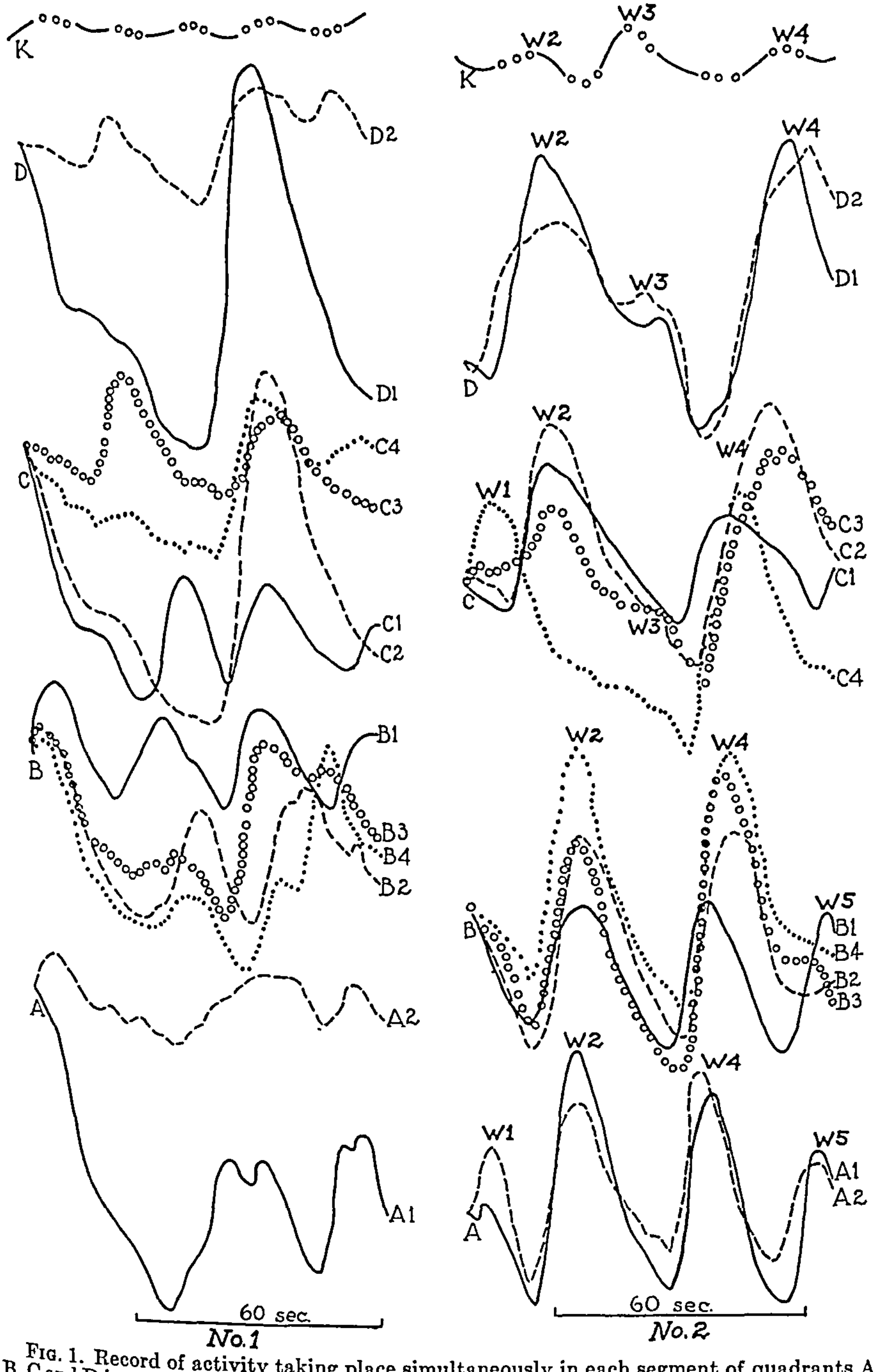

FIG. 1. Record of activity taking place simultaneously in each segment of quadrants A, B, C and D in exposed half of bladder during two periods of observation in same cat. Kymographic record (K) represents total bladder response during each period of observation.

No. 1, activity taking place when intravesical pressure was held constant at 4 cm. of water and initial volume was 33.4 cc.

No. 2, activity taking place under a constant pressure of 5 cm. of water with an initial volume of 36.9 cc. Periods of synchronous activity are indicated by waves W1, W2, W3, W4 and W5.

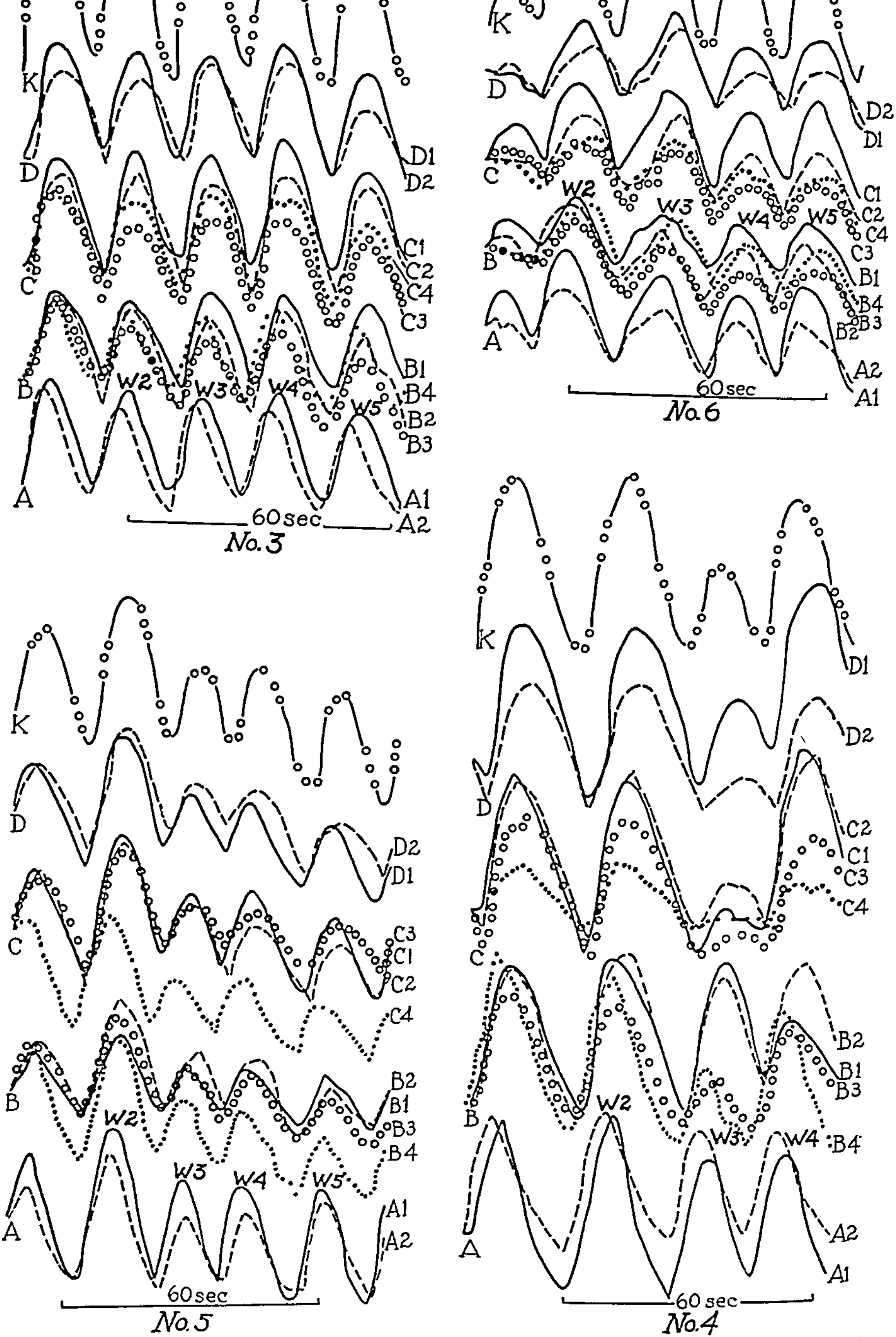

FIG. 2. Simultaneous recording of activity taking place in each segment of bladder during four periods of observation in same cat. W2, W3, etc., indicate synchronous waves of activity. For each period of observation, kymographic record (K) reflects total bladder response.

No. 3, activity taking place when intravesical pressure was held constant at 7 cm. of water and an initial volume of 35.4 cc.

No. 4, record of activity taking place when intravesical pressure was held constant at 5 cm. of water and the initial volume was 47.4 cc.

No. 5, record of activity taking place at constant pressure of 8 cm. of water and an initial volume of 48.4 cc.

No. 6, record of activity taking place at a constant pressure of 10 cm. of water and initial volume of 52.4 cc.

taneous activity in all parts of this bladder little synchronous movement could be observed. In quadrant A the segments of muscle acted quite independently. In quadrant B the rhythm exhibited by the different segments was irregular while in the more distal quadrants (C and D) some of the segments underwent shortening while others were relaxing. Thus the timed photographs revealed that the various segments of the bladder were very active even though the kymograph record (fig. 1, K) of the total bladder response was indicative of a relatively quiescent viscus displaying a simple rhythmic activity.

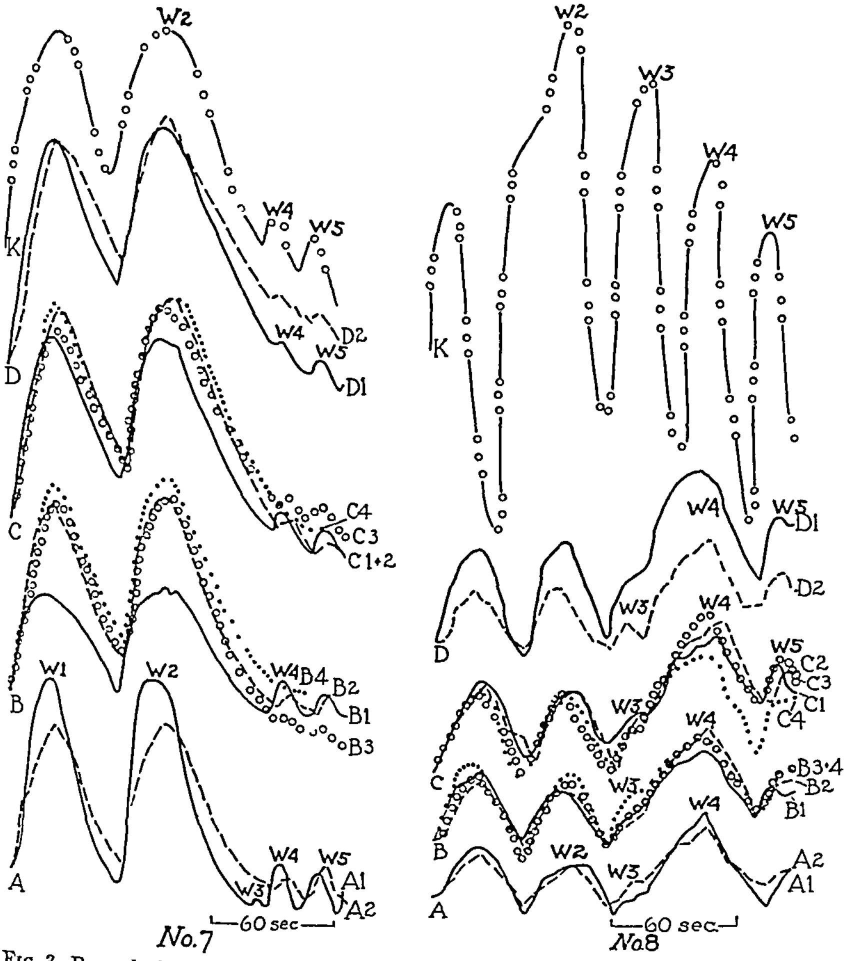

FIG. 3. Record of activity taking place simultaneously in each of the 12 segments of the bladder during two periods of observation. W2, W3, etc., indicate synchronous waves of activity. For each period of observation kymographic record (K) reflects total bladder response.

No. 7, record of activity when initial volume of bladder was 49.4 cc, and pressure was held constant at 8 cm. of water.

No. 8, record of activity in moderately distended bladder under moderate, variable pressure.

When the pressure was held constant at 5 cm. of water and the bladder contained an initial volume of 36.9 cc (fig. 1, No. 2), the muscle exhibited two slow rhythmic waves of activity. The one (W2) appeared in quadrant A eleven seconds after its appearance in the D quadrant while the other (W4) is almost the reverse of this with the onset of contraction in quadrant A and ending in quadrant D twelve seconds later. The other waves (W1, W3, W5) occur infrequently in one or another of the bladder quadrants. The kymographic record (K) gives little indication of such irregular waves of activity.

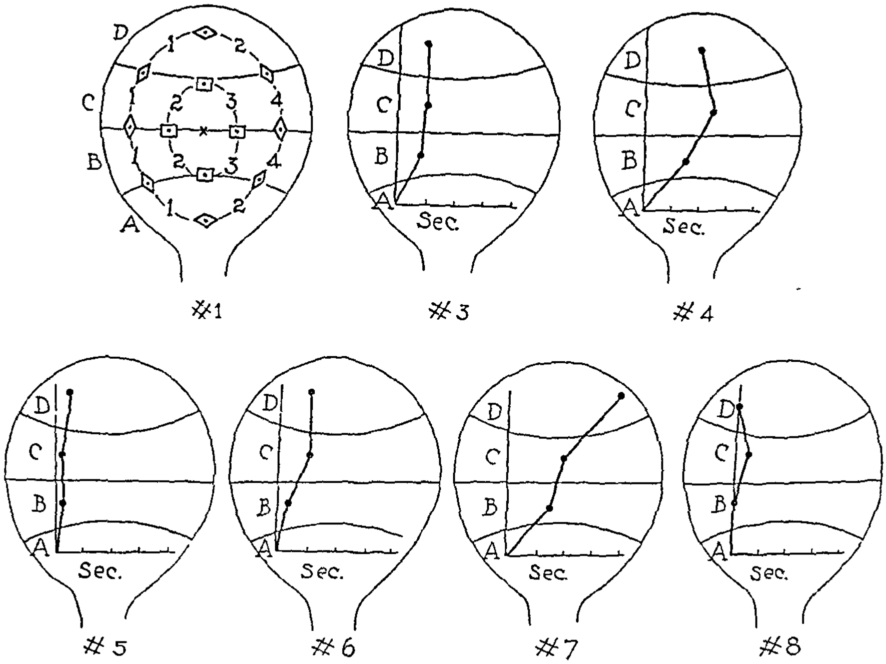

FIG. 4. No. 1, sketch of exposed surface of bladder showing location of segments and quadrants.

Nos. 3–8, each group shows time at which various quadrants of bladder begin to contract during a single wave of spontaneous activity. Below each graph is a number (3–8) indicating period of observation from which data were obtained.

Observation No. 3 (fig. 2) was recorded at a constant pressure of 7 cm. of water. The bladder had an initial volume of 35.4 cc. In this slightly distended viscus a series of waves of contraction (W2, W3, W4, W5) began in quadrant A. In each case the distal quadrants contracted from one-half to one second later (see fig. 4, No. 3 for graph of wave 2). According to Stewart's classification, the rhythm exhibited by this bladder is simple and regular in type.

The activity of the bladder when moderately distended by an initial volume of 47.4 cc at a constant pressure of 5 cm. of water is recorded in figure 2, No. 4. All the recorded waves of contraction (W2, W3, W4) originate in quadrant A one and one-half to five seconds before their appearance in the more distal quadrants of the bladder as shown by a graph of wave 2 (fig. 4, No. 4). Wave three (W3) was unusual in some respects. Although it was essentially peristaltic there appeared to be a local suppression of the wave in some areas. This was especially true of segments B3 and B4 of quadrant B, all segments of quadrant C and one segment (D2) of quadrant D. In these instances the amount of the contraction per unit length of muscle was greatly reduced. This irregularity is reflected in the kymographic record (K).

Another observation of the moderately distended viscus under constant pressure is recorded in figure 2, No. 5. Again there appeared to be a nodal point of activity in the proximal region of the viscus (wave 3, fig. 4, No. 5). There was also some tendency for all areas to contract in unison.

Observation No 6. (fig. 2) shows the activity pattern of a well distended bladder containing an initial volume of 52.4 cc at a constant pressure of 10 cm. of water. Synchronous waves of activity began in quadrant A and spread along the long axis of the viscus to the distal areas (wave 2, No. 6, fig. 4). In wave 4 of this bladder (fig. 2, No. 6) all quadrants contracted in unison.

Micturition was recorded in figure 3, No. 7. The initial volume of the bladder was 49.4 cc and the pressure remained constant at 8 cm. of water. The bladder was completely emptied by a peristaltic wave which began in quadrant A and reached the dome of the bladder 4 seconds later (fig. 4, No. 7). Three recovery waves were recorded (fig. 3, No. 7, W3, W4, W5). Of these wave 3 appears only in the A quadrant while waves 4 and 5 are definitely peristaltic with the nodal point of activity in the A quadrant. Each wave passes from the proximal to the more distal regions of the viscus in from four to five seconds.

Observation No. 8 (fig. 3) was of a moderately distended bladder under moderate and variable pressure. The nodal point of activity was variable. In wave 2 (fig. 4, No. 8) three quadrants contracted in unison while in other waves (fig. 3) a different pattern of contraction was discernable. Measurements from the timed photographs (fig. 3) indicate the presence of two separate rhythms but the kymographic record (K, fig. 3, No. 8) gave little indication of such an irregularity.

DISCUSSION

The data which have been presented indicate that all regions of the bladder exhibit spontaneous activity. In bladders which are but slightly distended there is a more or less unsynchronized writhing of the detrusor muscle. Even though individual regions of the bladder may show great activity, the kymographic record, which reflects the total bladder response, usually indicates a relatively quiescent bladder. This is accounted for by the antagonistic action of different regions or segments of the viscus. According to Denny-Brown and Robertson (1933), this unorganized type of behavior is due to a continual 'peppering' of the muscles by nervous impulses; but, as Gruber (1933) points out, most investigators have concluded that this form of activity is a property of the muscle itself. The opinion held by Langworthy et al. (1940) that the normal waves of micturition are unable to break through to initiate the emptying reflex in these slightly distended bladders is confirmed by our timed photograph procedure.

In bladders which are moderately to well distended an orderly wave of contraction is frequently observed. A given wave usually begins in the proximal region of the viscus and passes along the long axis of the bladder to the distal region. In most instances the contraction begins in the proximal region one to four seconds before the wave reaches the apex. This seems sufficient evidence for the presence of a pacemaker or a nodal point of activity in the proximal region of the viscus.

Micturition was observed in one experiment. While no conclusions can be drawn from such limited evidence, there are definite indications that in micturition there is a peristaltic wave of activity which begins in the proximal region of the bladder and extends to the more distal portions. This observation is not in agreement with that of Langworthy et al. (1940) who found that all portions of the bladder contract in unison during micturition. However, it does support Muellner's (1950) clinical observation that the first step in voluntary micturition is a downward tug in the region of the internal sphincter which is followed by contraction of the detrusor. Muellner reported that the contraction wave starts from the internal sphincter and spreads along the base upward to the sides and dome of the bladder.

Since the direction of this wave is opposite to that which one might expect, it seems more compatible with the fetal requirements for evacuating the bladder through the urachus into the allantoic sac. From this standpoint the pattern of activity of the adult detrusor muscle may be cited along with other fetal rudiments as an example of a physiologic vestige.

CONCLUSIONS

All regions of the urinary bladder in the cat exhibit spontaneous activity. In the small or slightly distended bladder this activity is irregular and uncoordinated, while in bladders which are moderately to well distended, there is usually a nodal point of activity in the proximal region which initiates a peristaltic wave of contraction which passes to the more distal regions. This was true also in micturition.

REFERENCES

Denny-Brown, D. and Robertson, E. G.: On the physiology of micturition. Brain, 56: 149, 1933.

Gruber, C. M.: The autonomic innervation of the genito-urinary system. Physiol. Rev., 13: 497, 1933.

Hegre, E. S. and Ingersoll, E. H.: An analysis of regional variations in the response of the detrussor muscle to electrical stimulation of the hypogastric nerves. J. Urol., 61: 1037, 1949.

Langworthy, O. R., Kolb, L. C. and Lewis, L. G.: Physiology of Micturition. Baltimore: Williams and Wilkins, 1940.

Muellner, S. R.: The physiology of micturition. Its clinical application. Bull. New Eng. Med. Center. 12: 93, 1950.

Stewart, C. C.: Mammalian smooth muscle: The cat's bladder. Am. J. Physiol. 4: 185, 1900.

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DEPARTURE FROM THE BAG CATHETER IN PROSTATECTOMY

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Since the beginning of prostatic surgery many devices and methods for the control of bleeding have been proposed. Innumerable references in the urologic literature offer a modification or other suggestion as to indicate concern among urologists for this problem.

The majority of the hemostatic methods have been in the form of packs or bag catheters to fill the prostatic fossa, and to control bleeding by compression.

In 1937, Foley presented the bag catheter as it is now generally used. This seemed to satisfy the need for improved hemostasis for a time, but there have been many subsequent suggestions indicating continued concern for this problem. The large bag catheters, with or without traction as some urologists advocate, afford great discomfort to some patients. The constant desire to urinate often requires narcotics and sedation for its control. The depressing action of narcotics on elderly patients is well known, and methods of hemostasis that do not produce urinary tenesmus are highly desirable.

During the evolution of prostatic surgery to its present standards too much emphasis has been placed on hemostasis by compression, and advantage has not been taken of the inherent ability of the prostatic capsule to contract and thereby control hemorrhage in that manner.

Our experience is based on the transurethral and retropubic approaches for prostatectomy. In cases of retropubic prostatectomy it was noted in the larger prostates that there was an immense distention of the capsule by the prostatic adenoma. Following enucleation of the adenoma there was a prompt contraction of the capsule, so that instead of the 12 to 15 sutures which would have been required to close the capsule if it had maintained its preoperative size, it could be closed with only 5 or 6 sutures. Also patients after transurethral resection have been returned to their beds with a bag catheter draining practically clear urine. Within a few hours, with disappearance of the anesthesia and sedation, the patient experienced marked vesical tenesmus and the drainage became increasingly bloody. In these cases the bag has been deflated and the catheter strapped to the penis with prompt relief of discomfort and a gradual cessation of bleeding.

These observations caused us to wonder whether we were not responsible for more bleeding by keeping the prostatic capsule dilated. Whereas, if we did not

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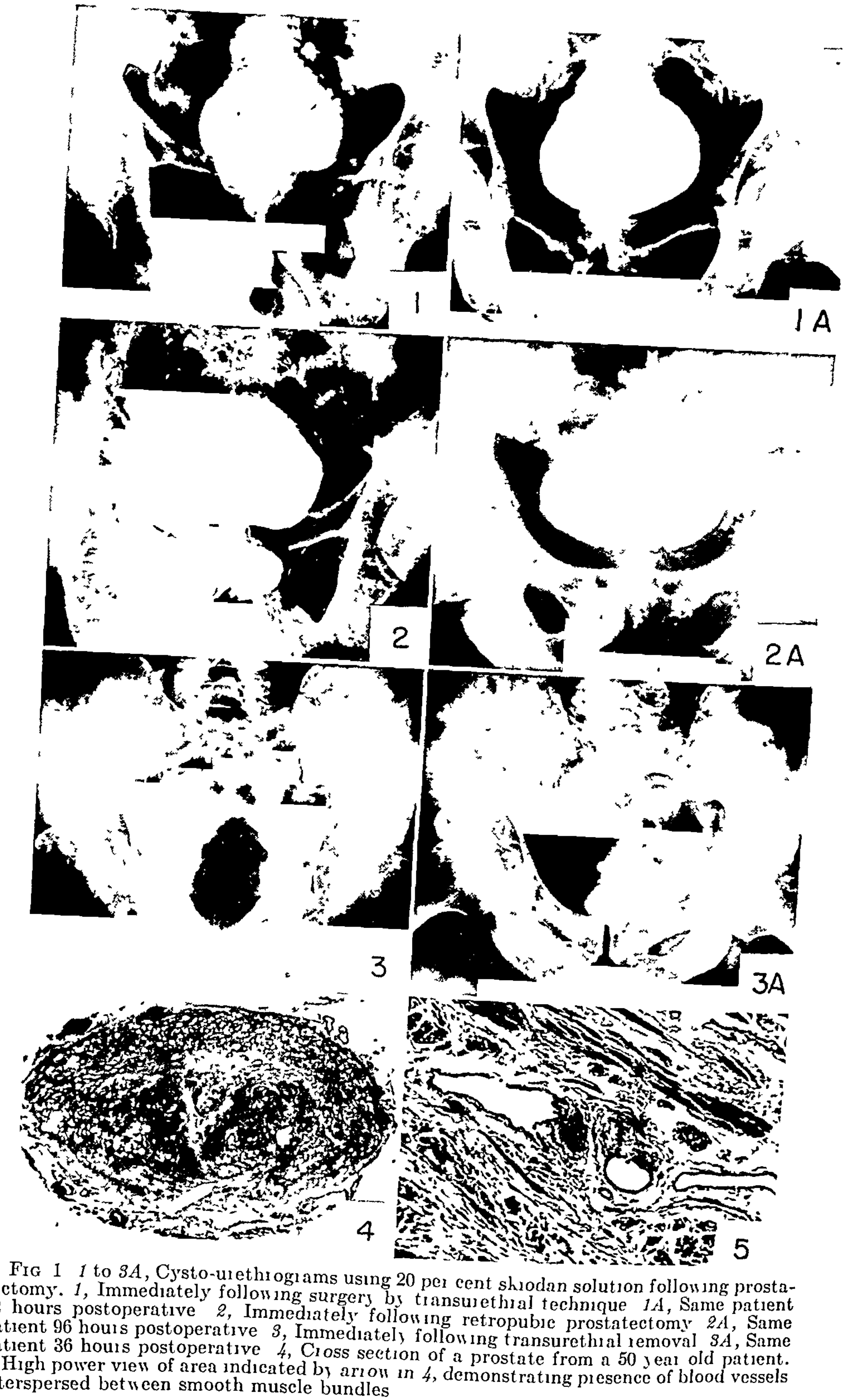

FIG 1 *1* to *3A*, Cysto-urethrograms using 20 per cent skiodan solution following prostatectomy. *1*, Immediately following surgery by transurethral technique *1A*, Same patient 12 hours postoperative *2*, Immediately following retropubic prostatectomy *2A*, Same patient 96 hours postoperative *3*, Immediately following transurethral removal *3A*, Same patient 36 hours postoperative *4*, Cross section of a prostate from a 50 year old patient. *5*, High power view of area indicated by arrow in *4*, demonstrating presence of blood vessels interspersed between smooth muscle bundles interfere with the inherent ability of the capsule to contract, there would be less postoperative bleeding and certainly more comfort to the patient.

The bladder neck and prostatic capsule have an abundance of smooth muscle which like all smooth muscle possesses the inherent properties of tonicity and resistance to extension. The prostate is invested in an outer fibrous sheath derived from the pelvic fascia. Within this sheath of the prostate is a true prostatic capsule which consists of a coat of interlacing fibromuscular tissue (fig. 1, *4* and *5*). Beneath this is a compressed layer of nonadenomatous prostatic tissue. As we all know, it is internal to this layer that the cleavage plane for the enucleation of the adenomatous prostate is established. Following the emptying of the prostatic capsule of its adenoma there is not a persistence of a large prostatic fossa. If the circular muscle fibers have been exposed over the entire circumference of the vesical neck, it will contract to its normal size of 26 to 30F within a few minutes after prostatectomy. The prostatic fossa also contracts immediately but not to the same degree as the bladder neck. The initial contraction of the prostatic fossa is approximately 50 per cent and further gradual reduction occurs over the next 12 hours. Reproductions of cysto-urethrograms are shown in figure 1, *1*, *1A*, *2*, *2A*, *3*, *3A*. The amount of capsular contraction is readily seen. Of course, to utilize this factor, there must be complete removal of the adenoma by whatever operative route, for remaining pieces of hypertrophied tissue will interfere with adequate contraction and result in hemorrhage. This mechanism of bleeding control is comparable to that of the uterus after being emptied of its foetus and placenta. Likewise, in this analogy, if there is incomplete removal of placenta tissue, it will interfere with adequate contraction and usually there will be hemorrhage.

As viewed in the knowledge of the description by Flocks of the blood supply to the prostate there is an anatomical reason for the effectiveness of this method. The predominant blood supply to the hyperplastic prostatic tissue is derived from the urethral division of the prostatic artery and this branch enters in the region of the vesical neck. The contraction of the bladder neck and prostatic capsule is a major factor in the control of bleeding in this area.

Morbidity and mortality in prostatic surgery are definitely influenced by loss of blood both at the time of surgery and in the immediate postoperative period. There is much emphasis placed on the amount of blood lost during resection in the operating room, and often too little consideration is given the blood loss after the patient returns to the bed.

The time to control bleeding is at the operating table. Prior to completion of a transurethral prostatectomy all bleeding points should be controlled by coagulation, and in retropubic prostatectomies by ligation. The draining fluid should be no more than pink tinged on completion. With the use of careful hemostasis at the time of operation, and if the inherent ability of the capsule to contract is not interfered with by a bag catheter, the postoperative bleeding is of little concern.

No effort has been made in this experience to measure accurately the blood loss, but the smoother convalescence and the noted decrease in the number of cases returned to the operating room for the control of bleeding are indicative of an improved management. The criteria on which this conclusion is based are summarized in table 1. It should be noted that this table includes data from 200 transurethral prostatectomies, 100 using bag catheter and 100 straight catheter. Of those patients returned to the operating room, bleeding was controlled by coagulation through the resectoscope under spinal anesthesia. In no patient has it been necessary to do a cystotomy for control of bleeding. It is notable that only 2, out of 50 patients with retropubic prostatectomy, were returned to the operating room for hemostasis. In these there was no leakage of irrigating medium through the sutured capsule during the procedure of clot evacuation and coagulation, even though it was less than eight hours after surgery.

Goodyear and Beard, in their study of blood loss in prostatectomy, found in a series of suprapubic prostatectomies that the hemostatic bag series lost almost twice as much blood as did a control series in which no hemostatic agent was used.

TABLE 1. *Comparison of series of 100 transurethral prostatectomies*

	100 CASES BAG CATHETER USED	100 CASES STRAIGHT CATHETER USED
Postoperative bleeding (return to O.R. for control)	17	3
Average number of days of hospitalization	12	9
Postoperative transfusions	50	18
Marked febrile reaction	35	10
Mild temporary incontinence	23	3

A bag catheter in transurethral resection cases is needed only when the capsule is invaded and a venous sinus is opened. In these, no amount of coagulation will control the bleeding. On completion, a bag catheter is distended in the fossa for 30 minutes, which is usually sufficient to control this type of bleeding, then deflated and strapped in place.

Drainage is not as free through the hemostatic bag catheter as it is through the two-eye, 22F, Robinson catheter. This delayed drainage in the presence of bleeding aids in the formation of clots requiring frequent irrigation, thus affording increased opportunity for contamination and subsequent infection. Irrigations are held to a minimum and frequently no irrigations are used the first 24 hours. This pumping action of the bladder by irrigation accentuates the bleeding.

There has been a noted decrease in the incidence of postoperative chills and fever since the use of a straight catheter has been instituted. A decrease in patients complaining of slight incontinence for a few days after surgery in the straight catheter series as compared with the hemostatic bag cases has also been noted.

SUMMARY

Satisfactory hemostasis is obtained in transurethral and retropubic prostatectomies if the inherent ability of the prostatic capsule to contract is not interfered with by a bag catheter, and the prostatic capsule is completely emptied of its adenomatous tissue.

A straight catheter has been substituted for the conventional bag catheter, with improved results. A comparison of a series of transurethral prostatectomies is made.

The structure of the prostatic capsule on which this concept is based is briefly discussed.

REFERENCES

Flocks, R. H.: Arterial distribution within the prostate gland; its role in transurethral prostatic resection. J. Urol., **37**: 524-548, 1937.

Goodyear, W. E. and Beard, R. E.: Blood loss in prostatectomy. J. Urol., **62**: 849, 1949.

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THE PROSTATIC SMEAR AND ITS CLINICAL USEFULNESS

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The clinical value of the cytologic examination of prostatic secretion has been investigated for several years. Its usefulness in the diagnosis of cancer has been stressed by some[1, 2] and disputed by others.[3] The interest in this method of examination will probably grow with the increasing knowledge of prostatic cytology[4, 5, 6] and the refinement of successful treatment of early carcinoma of the prostate. The chance of cure by radical surgery depends on the possibility of finding cancer of the prostate early, before this disease has spread. The addition of the prostatic smear interpretation to already available methods of examination (digital examination, chemical examination, cystoscopic examination, pathologic examination after biopsy and x-ray survey) is noteworthy if it enhances the possibility of correctly identifying prostatic disease. The survey of cells in the prostatic secretion can become an important part of diagnostic procedures, as it gives insight into cells and cell changes of the ducts of the prostate itself. It depends upon the fact that epithelium continually desquamates cells which if they are transferred on a slide and stained are recognizable under the microscope. Material obtained by direct prostatic massage contains cells desquamated from the urethra, the seminal vesicles, the ampulla, as well as from all those parts of the prostate which are connected with the urethra by patent ducts. The technique of obtaining material and preparing it for cytologic examination is simple and has been standardized. Fixing solutions and staining methods were described by Papanicolaou[7] for the vaginal fluid and later found suitable for the preparation of material from other body fluids. In order to be able to recognize cells from malignant lesions of the prostate a familiarity with cells in the prostatic smear obtained from patients who do not have a cancer is essential.

The *normal prostate* sheds few cells. The secretion expressed from a prostate of a young person shows only a very few rather small single columnar cells which are scattered over the slide.

Read at annual meeting, Northeastern Section, American Urological Association, Bolton Landing, N. Y., September 16, 1950.

This study was supported in part with funds from the Dr. Henry C. Buswell Memorial and carried out in the cytological laboratory supported by the Monroe County Branch of the American Cancer Society.

[1] Albers, D. D., McDonald, J. R. and Thompson, G. J.: Carcinoma cells in prostatic secretions. J. A. M. A., **139**: 299–303, 1949.

[2] Haschek, H. and Gutter, W.: The clinical value of cytology in early diagnosis of malignant disease of the prostate. Der Krebsarzt, **4**: 222–223, 1949.

[3] Boyer, W. F.: Carcinoma of prostate: A cytological study. J. Urol., **63**: 334–345, 1950.

[4] Herbut, P. A. and Lubin, E. N.: Cancer cells in prostatic secretions. J. Urol., **57**: 542–551, 1947.

[5] Jonsson, G. and Fajers, C. M.: Cancer cells in prostatic secretion. Acta Chir. Scan., **99**: 545–559, 1950.

[6] Peters, H.: The prostatic smear. Cancer, **3**: 481–487, 1950.

[7] Papanicolaou, G. N. and Traut, H. F.: Diagnosis of Uterine Cancer by the Vaginal Smear. New York: Commonwealth Fund, 1943.

Secretion obtained from a patient with *benign prostatic hypertrophy* shows many cells for study (fig. 1, *A*). The columnar cells are larger than those found in the normal prostate. They have clear homogeneous nuclei and ample cytoplasm. If they are desquamated in sheets they often show a honeycombed appearance as cell membranes are intact. Superficial squamous cells are easily recognized; they are large cells with small nuclei. Cells from the transitional epithelium of the urethra might appear in smears obtained from benign prostatic hypertrophy but they are usually rather few. Histiocytes and leukocytes are seen in varying numbers.

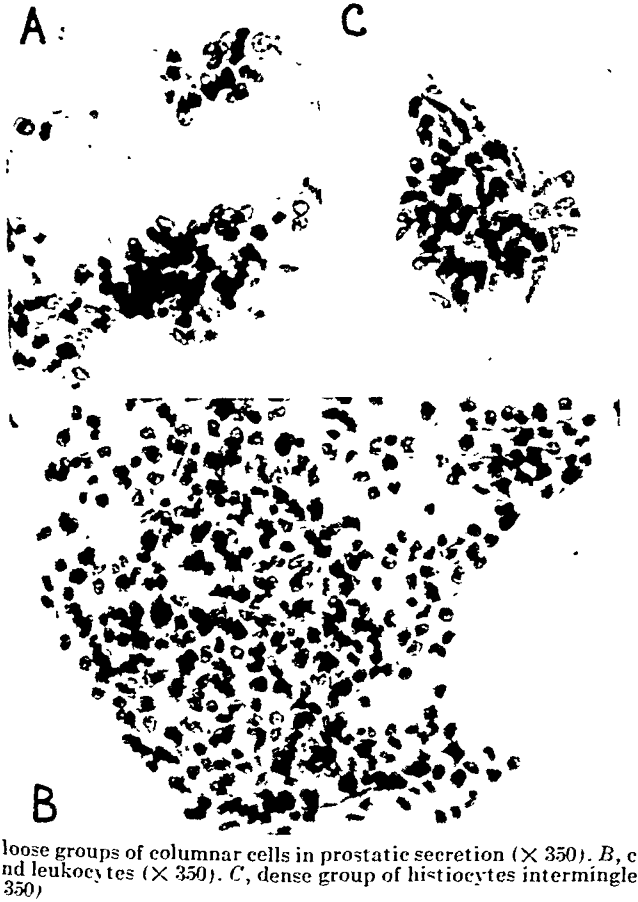

FIG. 1. *A*, loose groups of columnar cells in prostatic secretion (× 350). *B*, columnar cells, histiocytes and leukocytes (× 350). *C*, dense group of histiocytes intermingled with columnar cells (× 350)

The prostatic smear prepared from a patient with *prostatitis* is usually rich in desquamated cells. Large numbers of inflammatory cells, neutrophilic as well as eosinophilic leukocytes, are intermingled with epithelial cells (fig. 1, *B*). The columnar cells are found in dense groups showing various stages of degeneration. Their nuclei may be completely degenerated and just be represented by irregularly outlined black masses. Histiocytes of many forms and shapes may compli-

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[3] Boyer, W. F.: Carcinoma of prostate: A cytological study. J. Urol., **63:** 334–345, 1950.

[4] Herbut, P. A. and Lubin, E. N.: Cancer cells in prostatic secretions. J. Urol., **57:** 542–551, 1947.

[5] Jonsson, G. and Fajers, C. M.: Cancer cells in prostatic secretion. Acta Chir. Scan., **99:** 545–559, 1950.

[6] Peters, H.: The prostatic smear. Cancer, **3:** 481–487, 1950.

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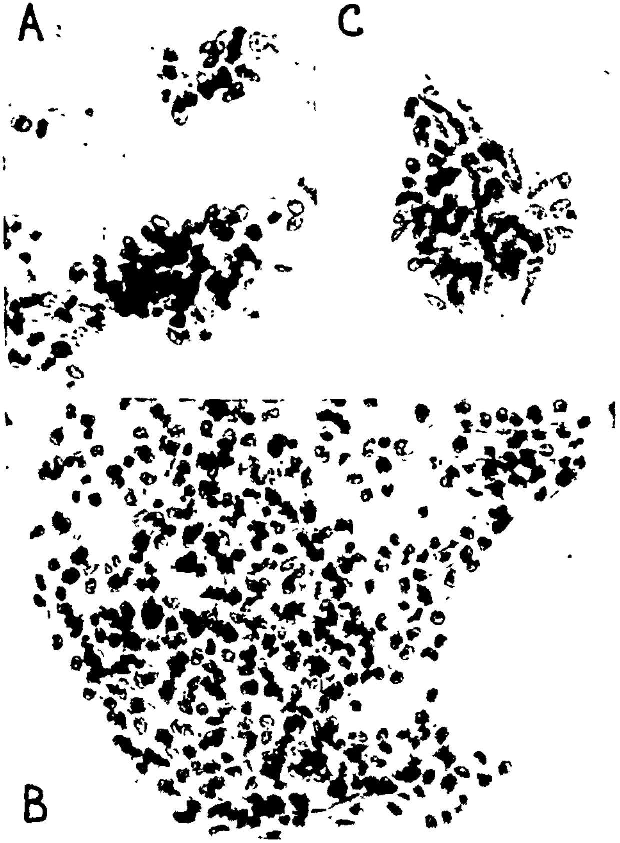

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The *"seminal vesicle smear"* shows completely different characteristics from the types of smear just discussed (fig. 2). The material seen on these preparations is probably expressed by stripping of the seminal vesicles. Spermatozoa make up a large part of the cell population. They can be distributed so densely that they obscure all other cell elements. The epithelial cells seen in these smears are small cells with large uniformly dark staining nuclei which might take on rather bizarre forms. These cells made interpretation of smears at first uncertain and difficult until we were able to identify them as coming from the seminal vesicles. They were found in smears prepared by direct contact with seminal vesicles removed at surgery or autopsy but were not seen in contact smears prepared from removed prostates. Epithelial cells in the seminal vesicles are characterized by their atypia which is well known to the pathologist. They are found in massaged specimens singly as well as in loosely arranged groups. Some of them contain a pigment but, unfortunately, the pigment is not found in all of these cells which would make their identification extremely simple.

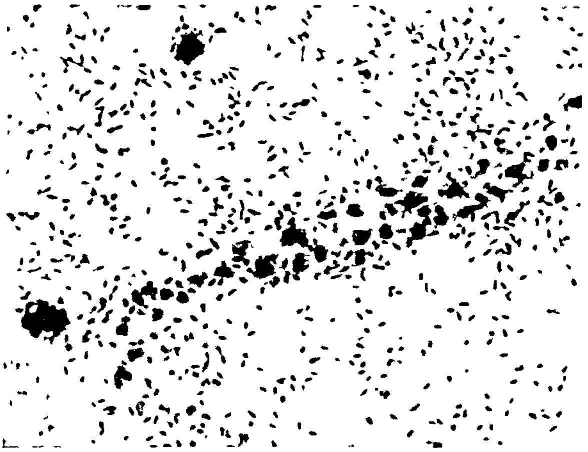

FIG. 2. Spermatozoa and epithelial cells in "seminal vesicle smear" (× 350).

FIG. 3. Histiocytes with spermatozoa (× 350).

The most characteristic cell in the seminal vesicle smear is the histiocyte,

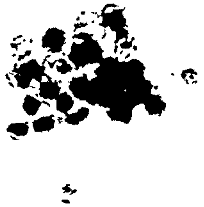

FIG. 4. Malignant cells in loose groups showing variation in nuclear size and prominent nucleoli (× 350).

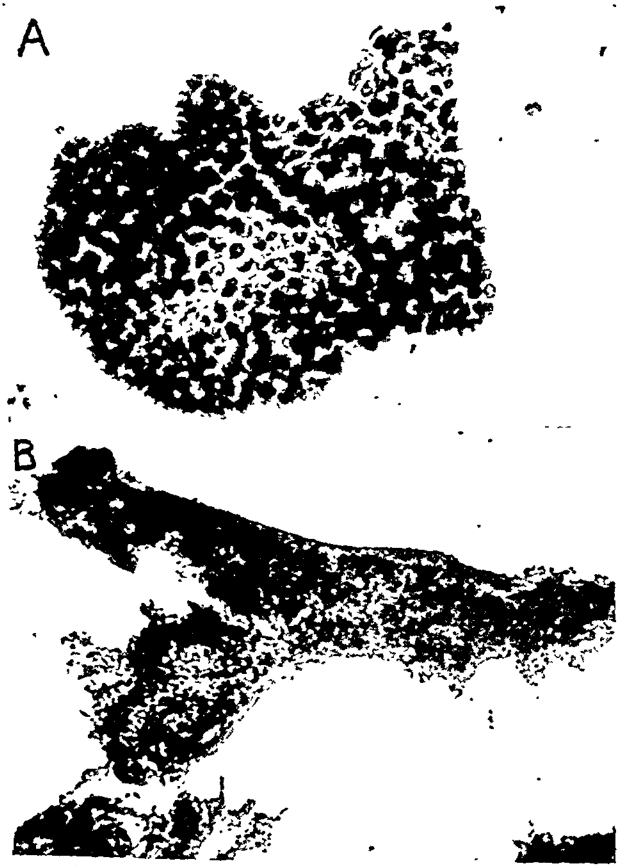

FIG. 5 *A*, group of cancer cells, "cast-like" formation (× 350). *B*, large sheet of cancer cells (× 100).

showing phagocytic activity (fig. 3). It is a fairly large round cell with an eccentrically placed, often kidney shaped, nucleus. Varying numbers of spermatozoa can be engulfed in these cells. If they are only a few the identity of the cell is maintained. However, the spermatozoa might form dense masses within these cells and be mistaken for abnormal cells. At times smears obtained by stripping of the seminal vesicles will contain some cells coming from the prostate, but usually we fail to find cells desquamated from the prostate and have therefore to reject these slides as they do not represent the prostatic cell population.

Cells found in smears of patients who have *carcinoma of the prostate* are usually plentiful, varied and characteristic. They appear in loosely arranged groups (fig. 4) or they may form castlike structures (fig. 5, *A*). Occasionally very large sheets of cancer cells appear in the smear (fig. 5, *B*). The individual cell shows a disturbance in the nuclear-cellular ratio: the nucleus at times seems to fill the whole cell, making the recognition of cytoplasm difficult or impossible. The nuclei show variation in size within the same group, some reaching outstandingly large proportions. They are hyperchromatic, showing chromatin patches and large and multiple nucleoli (fig. 6, *A*) or they may be so deeply staining that details cannot be identified. This is especially true in the center of a cast-like structure, though on its periphery there are usually well preserved nuclei which show clearly the characteristics of malignant cells (fig. 6, *B*). The cellular borders are ill defined and cells have a tendency to cluster. Large cytoplasmatic vacuoles often appear in the clusters. Other cells are found intermingled with the cancer cell groups, depending on the pathologic picture of the prostate. Groups of columnar cells will be shed from hypertrophic parts of the gland. Histiocytes, leukocytes and erythrocytes will be found in varying numbers depending upon the amount of infection present.

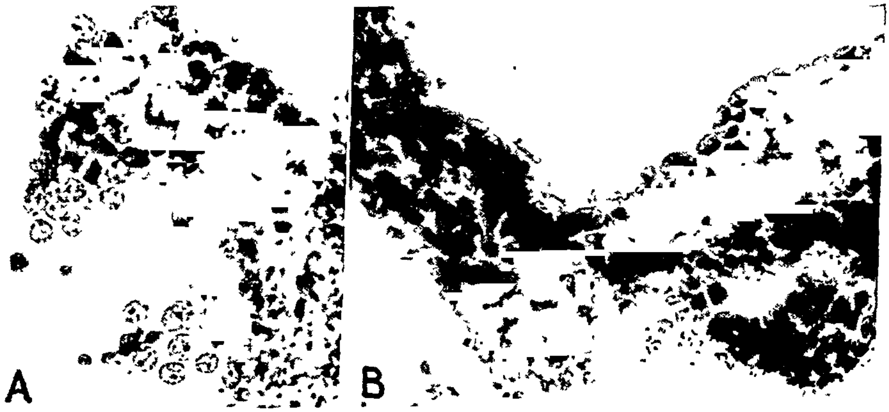

Fig. 6. *A*, cancer cells showing hyperchromatism and prominent and multiple nucleoli (× 350). *B*, dense group of cancer cells with cells showing characteristic nuclear detail at periphery (× 350).

The study of cells in the prostatic smear so far has been used for diagnostic purposes only, but it seems to have another value in the practice of urology: It can be used as a guide in hormonal treatment of carcinoma of the prostate.

Clinically, it is well established that a prostate harboring a cancer will change its size and consistency during estrogen therapy or after orchiectomy—at least for a while. The big stony hard gland changes to a smaller, softer organ. Huggins[8] and others have shown that carcinoma of the prostate will regress and remain latent for a time under estrogen therapy. Kahle, Schenken and Burns[6] demonstrated the cellular changes in histologic sections that take place in carcinoma of the prostate after estrogen therapy. They showed that the cancer cells undergo nuclear and cytoplasmatic regression under hormone therapy.

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[8] Huggins, C.: Endocrine substances in treatment of cancer J. A M. A., **111**: 750–754, 1949.

If patients with carcinoma of the prostate who are taking estrogen medication are followed at regular intervals with prostatic smears, characteristic changes can be observed in the cancer cells as well as in the rest of the cell population (fig. 7). The changes in the cancer cells make their identification often uncertain. The characteristics of the malignant cells become indistinct. The nuclei are still crowded and overlapping but their chromatin detail is lost. They stain uniformly dark and their interpretation as malignant cells rests with the appearance of the whole group.

FIG. 7. At right a group of malignant cells in which nuclear detail is lost ("altered" malignant cells); at left a group of glycogenic cells. Smear from a patient with carcinoma of the prostate receiving estrogen medication (X 350).

If smears are examined from patients who have been under continuous estrogen therapy for some time even these "altered" malignant cells are not found anymore. The cells that are seen are large superficial squamous cells which appear in vast numbers after hormone medication. They increase from an occasional one before therapy to overwhelming numbers. Perhaps the most characteristic cell that appears in the smear after estrogen therapy is started is the so-called glycogenic cell which is not seen before therapy is begun and which disappears quite promptly after the patient stops his medication. It is a round or oval cell which appears singly or in large groups and which on special staining proves to be filled with glycogen.

The question arose whether these glycogen filled cells come from the prostate itself. Direct smears prepared from prostates removed at surgery from patients with carcinoma who had received estrogen showed these glycogen filled cells. Histologic sections showed marked metaplasia of the cells lining the acini (fig. 8). Cells lying freely in the glandular spaces showed the same characteristics of

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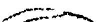
[6] Kahle, P. J., Schenken, J. R. and Burns, E. L.: Clinical and pathologic effects of diethylstilbestrol and diethylstilbesterol dipropionate on carcinoma of prostate gland. J. Urol., 50: 711-732, 1943.



those found in the smear. We, therefore, believe that the glycogenic cells seen in the smear come from the prostate itself and are desquamated from the metaplastic areas.

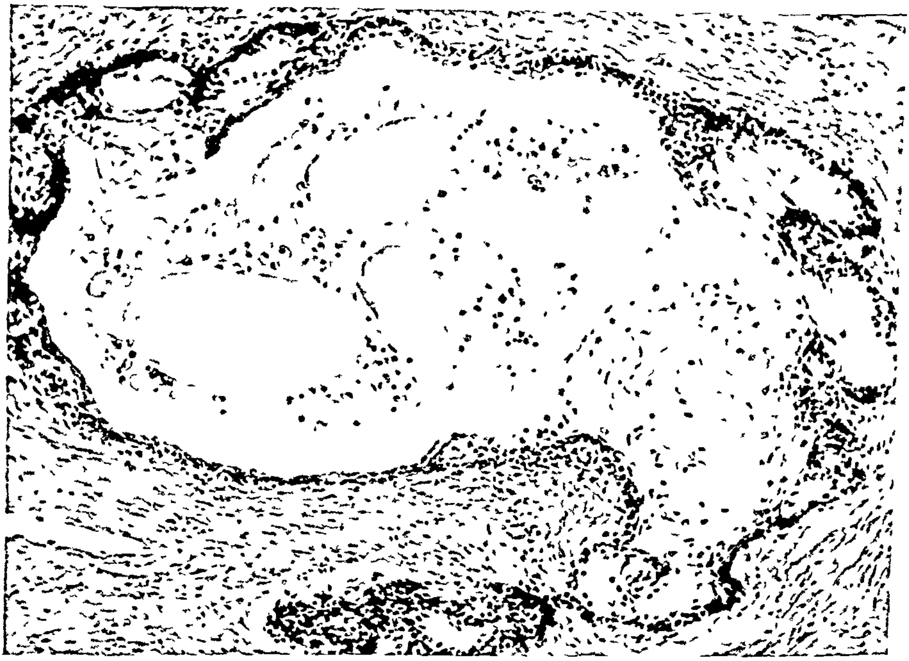


FIG. 8 Prostate, histologic section Marked squamous cell metaplasia Patient had taken estrogens continuously for 12 weeks (× 150)

TABLE 1. *Clinical and cytologic findings*

HISTOLOGIC OR CLINICAL DIAGNOSIS	NUMBER OF CASES	PROSTATIC SMEAR		
		Positive	Negative	Suspicious
Carcinoma	72	63	3	6

TABLE 2. *Patients with carcinoma of the prostate during estrogen therapy*

CLINICAL RESPONSE	NUMBER OF PATIENTS	PROSTATIC SMEAR	
		Malignant Cells Degenerated or Disappeared	"Unaltered" Malignant Cells Persist
Good	11	8	3
Poor	7	0	7

RESULTS

The prostatic smears used in this study came from 341 different patients seen in the Division of Urology at the University of Rochester School of Medicine. Among these were 72 patients who had carcinoma of the prostate (table 1). Half of these cases had confirmatory histologic sections. The other half were clinically diagnosed as having cancer. They either had extension to neighboring organs or elevated phosphatases values or x-ray evidence of metastases. Of these

72 cases with carcinoma, 63 prostatic smears contained malignant cells. Six smears were suspicious for malignancy and three failed to show characteristic cells (false negatives). One of these false negative smears on review was found to contain one suspicious group that was overlooked on first examination. Among the smears from 341 patients there was one false positive. The smear on this patient was reported as containing malignant cells. The histologic sections showed benign prostatic hypertrophy. Of the 72 patients who later proved to have carcinoma, three were not suspected of having the disease when first seen. In these cases the prostatic smear was of immeasurable help in bringing the true nature of the disease to light earlier than would have been possible if cytologic examination had not been made.

Several patients who had carcinoma and were taking estrogen medication were followed with prostatic smears taken at intervals. Of these, 18 patients were observed long enough to give at least a preliminary report on the usefulness of the prostatic smear in cancer therapy (table 2). Eleven patients responded well to hormone therapy. Their prostates decreased in size and changed from a stony hard induration to a softer consistency. The smears in 8 of these patients showed either characteristically degenerated cells or if the period of observation had been long enough, a disappearance of the malignant cells. The smears of 3 patients in whom the clinical response was good continued to show unaltered malignant cells. The clinical significance of this persistent shedding of malignant cells is not yet known. In 7 cases the clinical response to therapy was poor. The prostate did not show any change in consistency or size. All smears in these patients continued to show malignant cells which suggested a failure of the prostatic cancer to respond to hormone therapy.

This group of patients with carcinoma whose prostatic smears were examined periodically is still very small. It seems, however, to indicate that changes in the cell population of the prostatic secretion or the failure of these changes to occur gives an indication of the response of the cancer to hormone medication. If these described changes should be confirmed by a larger series of cases, they might perhaps be used in addition to other diagnostic measures as a guide in therapy. They may indicate when a larger dose of estrogen is necessary, a change of therapy is indicated or suggest the optimum time for surgery.

SUMMARY

Cancer of the prostate sheds cells into the prostatic secretion which are sufficiently characteristic to be recognized microscopically. Of 341 patients surveyed in this series, 72 had carcinoma of the prostate. The smears of 63 of these patients showed malignant cells to be present, 6 contained cells suspicious of malignancy and 3 failed to show characteristic cells. One false positive was reported in the 341 cases. Cell changes in smears from patients with carcinoma under estrogen therapy are described and the findings suggest that they may be used as an additional guide to therapy. The cytologic examination of prostatic smears has been found to be a useful addition to the methods of diagnosing carcinoma of the prostate.

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GENITAL TUBERCULOSIS IN THE MALE; A CONCEPT OF ITS PATHOGENESIS AND TREATMENT

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The purposes of this paper are threefold: to review critically the data presented by pathologists and urologists on the pathogenesis of genital tuberculosis in the male; to outline the forms of treatment dictated by the conclusions drawn from such a review, and to present the results of this treatment in 10 patients studied since 1940.

Interest in the subject was aroused late in 1939 by a review of fifteen cases of urogenital tuberculosis observed on the urology service of Freedmen's Hospital over a period of 8 months. Among these were 9 cases of genital tuberculosis, most of which had clinical evidence of active extragenital disease, but 3 were patients 25, 28 and 31 years of age who complained of unilateral tuberculous epididymitis without clinically demonstrable tuberculosis elsewhere, except for an ischiorectal abscess in the oldest patient. The desire for the most effective rehabilitation of these patients led to a careful review of the data then available on the subject.

A critical review of these data revealed many facts which had served as the bases for the formulation of conflicting opinions on the pathogenesis of genital tuberculosis and on the most desirable forms of treatment.

INCIDENCE

Genital tuberculosis in the male was found to occur most commonly in the third and fourth decades[1] in the form of tuberculous epididymitis associated with pulmonary tuberculosis.[1, 2, 3, 4, 5] It may occur with[1, 3, 6, 7, 8, 9, 10, 11, 12] or without[3, 7, 8, 9] clinically demonstrable tuberculosis of other organs.

CLINICAL ONSET

The clinical evolution of tuberculous epididymitis ranged from the extremes of: 1) an acute onset with pain, swelling, hyperpyrexia and tenderness, simulating gonorrheal epididymitis, and 2) an insidious onset consisting of a painless swelling which the patient noticed for the first time quite accidentally due to slight trauma or because of the spontaneous rupture of an existing suppuration.[3]

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[1] Kretschmer, H. L.: Surg., Gynec. & Obst., **47:** 652, 1928.
[2] Bothe, A. E.: Internat. Clinic, **2:** 158, 1938.
[3] Bumpus, H. C. and Thompson, G. J.: Surg., Gynec. & Obst., **47:** 791, 1928.
[4] Negley, J. C.: Tr. West Br. Soc. Am. Uro. Assn., **4:** 87, 1935.
[5] Quinby, W. C.: J. A. M. A., **71:** 1790, 1918.
[6] Cunningham, J. H., Jr.: Surg., Gynec. & Obst., **23:** 385, 1916.
[7] Sweany, H. C.: J. Urol., **29:** 217, 1933.
[8] Walker, K. MacF.: Lancet, **1:** 435, 1913.
[9] Young, H. H.: Arch. Surg., **4:** 334, 1922.
[10] *Braasch, W. F.:* Trans. Am. Assoc. Gen. Urin. Surg., **13:** 272, 1920.
[11] Lee and Bowes: Brit. J. Surg., **21:** 456, 1934.
[12] Scholl, A. J., et al: Arch. Surg., **34:** 754, 1937.

GENITAL LESIONS

In the acute cases there was usually an associated hydrocele. Examination revealed a tender swelling in the tail of the epididymis which spared the testicle; frequently there was some induration and tenderness of the vas; the prostate and seminal vesicles showed more advanced findings on the homolateral side, such as swelling, tenderness, nodular induration, softening and fluctuation.[1, 3, 6, 7, 8, 9, 10]

In chronic cases the oldest lesion was outlined as a firm, soft or fluctuant swelling in the tail of the epididymis or it spread into the dartos as a large and doughy mass with areas of fluctuation. If a draining sinus had developed, its lumen usually led to the tail of the epididymis. Other possible findings were: discrete globular swellings of the body or head of the epididymis; massive or lesser involvement of the testis; homogeneous enlargement and induration or localized bead-like sclerosis of the vas and clinically demonstrable involvement of the prostate, seminal vesicles, vas and epididymis on the contralateral side.[1, 3, 6, 7, 8, 9, 10]

ASSOCIATED EXTRAGENITAL LESIONS

Pulmonary tuberculosis was the most common form of the infection in the age group in which tuberculous epididymitis occurred most frequently.[1, 2, 3, 4, 5] Only 2 per cent to 5 per cent of male patients with pulmonary tuberculosis developed tuberculous epididymitis,[2, 1, 6, 13, 14] but an active pulmonary tuberculous infection was found on an average of 63.7 per cent of patients with tuberculous epididymitis.[1, 2, 3, 4, 5] Similarly, renal tuberculosis was recognized clinically in 49 per cent of these patients,[1, 3, 4, 6, 11, 12] involvement of the seminal vesicles in 62 per cent,[6, 15, 16] of the prostate in 68 per cent,[2, 6, 7, 9, 13] and combined prostatoseminal vesicle involvement in 73 per cent.[1, 3, 4, 6, 9, 10, 12] Far less frequently genital tuberculosis was associated with clinical tuberculosis in other organs and systems.[1, 3, 6, 7, 8, 9]

CLINICAL COURSE

Regardless of the type of the onset, whether acute or insidious, in most patients the disease showed a strong tendency to progress with eventual involvement of the entire genital tract. Whereas this was particularly true in patients whose disease was neglected or received only medical treatment, it was also true of many who received surgical treatment, consisting of the removal of unilateral diseased tissues from the scrotum. In these, section of the opposite vas reduced the incidence of contralateral epididymitis from 39 per cent to 10 per cent.[1, 3, 4, 5, 6, 9, 11, 15, 17, 18, 19]

[13] Bothe, A. E.: J. Urol., **18:** 494, 1927.
[14] Lowsley, O. S. and Duff, J.: Ann. Surg., **19:** 106, 1930.
[15] Keyes, E. L.: Ann. Surg., **45:** 918, 1907.
[16] Moore, R. A.: J. Urol., **37:** 372, 1937.
[17] Cecil, A. B.: Surg., Gynec. & Obst., **50:** 624, 1930.
[18] Robertson and Singer: Urol. & Cutan. Rev., **42:** 754, 1938.
[19] Wells, C. A.: Brit. J. Urol., **10:** 114, 1938.

PATHOGENESIS

Almost without exception, genital tuberculosis was found to occur as a secondary infection, resulting from the spread of the specific cause from a primary infection elsewhere in the body. The obvious avenue of spread from the usual sites of primary infections to the genital tract was the blood stream. Support for the belief in the hematogenous origin of genital tuberculosis was found in the discovery of isolated tuberculous lesions in prostates removed from clinically nontuberculous individuals[1, 13, 20, 21, 23, 24] and from the discovery of similar lesions in prostates, seminal vesicles, and epididymes obtained at autopsy.[1, 6, 7, 8]

Careful studies had made it clear that on a hematogenous basis patients could develop both clinical and subclinical tuberculous lesions of the kidneys.[19, 22] Moreover, the merging of the genital and urinary passages in the posterior urethra of the male was the obvious and accepted cause for the spread of infections from one tract to the other, notably the development of tuberculosis of the prostate, seminal vesicles and epididymes in patients with clinical renal tuberculosis.[8, 19] Similarly the spread of tuberculous infection from one epididymis to the other was believed to occur by way of the vasa, seminal vesicles and prostate.[3, 6, 8, 17, 18] In the face of these facts and beliefs, it was maintained that isolated tuberculous epididymitis evolved locally as a hematogenous implantation.[2, 3, 6, 8, 17, 18] A late dissenting opinion[19] held out the possibility that tuberculous epididymitis could develop through the vas without involving the prostate or seminal vesicles in patients with tuberculous bacilluria from subclinical renal tuberculosis.

DIAGNOSIS

Clinical evaluation of the extragenital tuberculous lesions, when present, and the identification of the genital lesions did not offer serious difficulty.[2, 3, 4, 6, 7, 9, 10, 12, 13, 14, 16] In the absence of a well-defined symptom complex it was not possible to identify tuberculosis of the prostate and seminal vesicles as isolated lesions,[24] yet, on physical examination of patients with either renal tuberculosis or an inflammation of the epididymis believed to be tuberculous, it was possible to detect the involvement of these organs when present.[15, 25, 26, 27]

TREATMENT

The plan of treatment adopted in each case was dictated by an evaluation of the character and extent of the extragenital as well as of the genital lesions. In patients with dominant extragenital disease, this was attacked primarily, using medical and surgical means in keeping with the best practices of the day, and leaving the genital lesions for secondary consideration and treatment.[3, 18] The genital

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[20] Bell, J. G. Yates: Brit. J. Urol., **9:** 114, 1937.
[21] Rolnick, H. C.: Surg., Gynec. & Obst., **41:** 15, 1925.
[22] Medlar, E. M.: Am. J. Path., **2:** 401, 1926.
[23] Townsend, W. G.: N. Eng. J. Med., **200:** 1085, 1929.
[24] Barney, J. D.: J. A. M. A., **63:** 2274, 1914.
[25] Young, H. H.: J. A. M. A., **104:** 722, 1935.
[26] Young, H. H.: Surg. Clinics North Amer., **16:** 1239, 1936.
[27] Whiteside, G. S.: Trans. Am. Assoc. Gen. Urin. Surg., **9:** 173, 1914.

disease was treated surgically, using either conservative or radical measures.[6, 9, 10, 26, 27, 28, 29]

The conservative treatment, including simple drainage, vasotomy with irrigation, epididymectomy and castration,[3, 6, 9, 10, 29] carried an insignificant immediate mortality from miliary spread, meningitis and peritonitis, and a remote mortality estimated to be about 20 per cent.[1] The benefits claimed for this form of surgery included: 1) removal of suppuration; 2) healing of sinuses, though at time long delayed; 3) subsidence of disease in the seminal vesicles and prostate, and 4) a cure rate estimated to be from 50 per cent to 60 per cent.[1, 6, 13 15, 20, 30] The radical operations introduced in the last decade of the ninteenth century aimed at the removal of the tuberculous foci in the vas and seminal vesicles by extending the incision along the vas retroperitoneally to the seminal vesicle. Later a midline suprapubic incision was made for better exposure,[9, 28] and still later Young perfected the perineal approach which permitted partial resection of the prostate.[24, 28] These more radical operations offerred the advantages of a complete recovery in a significant number of patients[6, 9, 11] and the removal of the remote mortality from genital tuberculosis.[9, 15, 16, 24, 26, 27, 28, 29, 30] They had the disadvantages of introducing a definite operative mortality[6, 11, 15] and of producing in new locations, fistulas which were very difficult to control.[21, 30] These disadvantages coupled with the specialized techniques required by these more extensive operations limited their use to a small number of urologists and only in those patients with clinical evidence of disease in the prostate and seminal vesicles.

CRITICAL EVALUATION

The authoritative opinion available in 1940 dictated for patients with tuberculous epididymitis a form of treatment consisting of the surgical removal of their unilateral tuberculous disease and section of the contralateral vas, to be followed by surgery of their seminal vesicles and prostate if the subsequent clinical findings indicated such a course. This form of treatment was based upon the concept of the pathogenesis of genital tuberculosis in the male which was widely held at that time.[1, 6, 7, 13, 20, 21] Indeed, if tuberculous epididymitis were due solely to hematogenous implantations, removal of such solitary foci would be the indicated treatment and it would be curative. However, clinical experience proved otherwise, for spread to the contralateral side, with and without clinically evident involvement of the seminal vesicles and prostate, was an entirely too common occurrence.[1, 3, 4, 5, 11, 15, 29] If, however, tuberculous epididymitis developed as a rule from disease of the prostate and seminal vesicles and involvement of these organs resulted from subclinical infections of the urinary system, the eventual bilateral involvement of the epididymis would be but a natural expression of the progression of the disease, unless this primary involvement of the genital tract were removed. Such a premise appeared to be in keeping with the

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[28] Whiteside, G. S.: Northwest Med., 18: 83, 1919.
[29] Young, H. H.: Surg., Gynec. & Obst., 26: 375, 1918.
[30] Osgood, A. T.: Am. J. Surg., 5: 215, 1928.

factual data available in 1940 and served as the basis for the decision to devise a radical form of treatment for the three male patients alluded to above who complained of unilateral tuberculosis of the genital system.

NEW RADICAL TREATMENT

The treatment of genital tuberculosis, to be successful, must take into account the patient as a whole, not merely his genital lesions. In patients with extragenital as well as genital tuberculosis, fine clinical judgment must dictate whether the genital disease must be ignored for the moment, should receive conservative surgical treatment, or may be removed in its entirety. This paper, however, is not concerned with the care of tuberculous patients with genital lesions. It is concerned with the treatment of genital tuberculosis in male patients without demonstrable extragenital tuberculosis or with such a disease under control, who complain of unilateral disease.

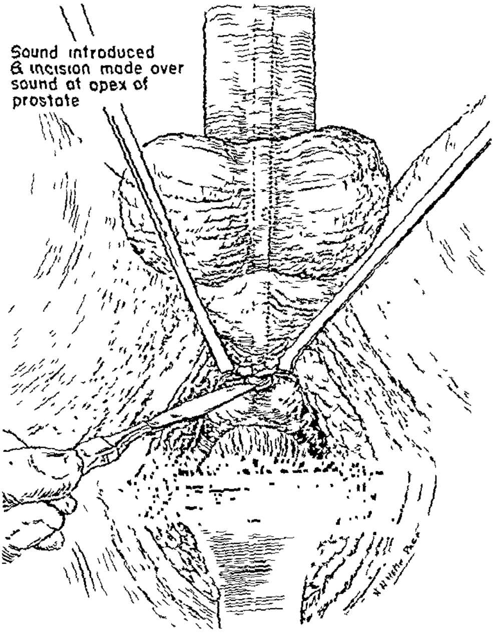

Sound introduced & incision made over sound at apex of prostate

FIG. 1. Perineal exposure of prostatic capsule. Incision through prostatomembranous urethral junction.

The surgical form of treatment devised for and recommended to these patients was based upon the premise that their disease began as an infection of the prostate and seminal vesicles, due to subclinical renal tuberculosis, and spread through the vasa to involve the epididymis. Accordingly, it differed from the forms of treatment devised by other urologists in that it had as its initial objective the removal of not merely the obvious tuberculous lesions in the scrotum, but also the parent lesions in the genital tract—those in the prostate, seminal vesicles and vasa.

The disease in the scrotum was treated by epididymectomy or castration, whichever was indicated by the extent of the pathological process. The vas on each was sectioned through a small incision over the external inguinal ring and its proximal part on the disease side was removed through the scrotal incision.

The prostatic capsule was exposed through a perineal approach. The urethra was severed just distal to the prostate (fig. 1). The capsule of the prostate was freed anteriorly by blunt dissection and the gland retracted posteriorly, exposing the anterior surface of the bladder neck. This was sectioned (fig. 2). The prostate was retracted posteriorly and, by blunt dissection, the ampullae of the vasa, and seminal vesicles were separated from the bladder and freed. By means of blunt dissection, gentle traction with torsion and bimanual manipulations at the inguinal and perineal incision, the distal portions of the vasa were completely mobilized and removed together with the prostate and seminal vesicles. The urethra was reconstructed over a rubber catheter by suturing the membranous urethra to the bladder neck (fig. 4). In later operations, the bladder neck was sutured to the superior layer of the urogenital diaphragm about the catheter and retention sutures were added to bind the posterior lip of the bladder neck to the perineal muscles (fig. 5). The wounds were cleaned with copious irrigation and their closure either with or without drainage was an individual matter.

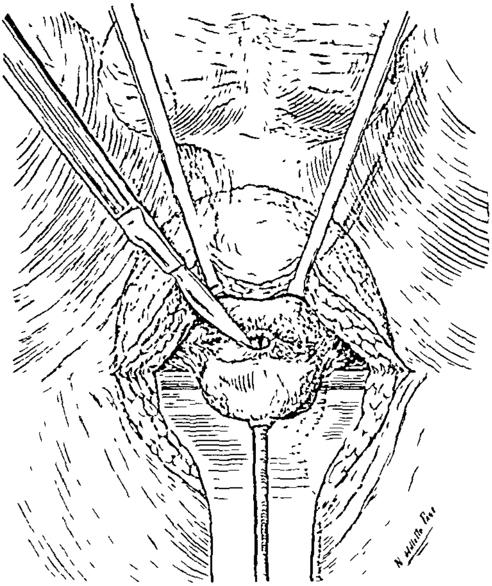


FIG. 2. Prostate with its capsule retracted downward after its anterior surface is freed. Incision through prostatovesical junction.

CASE REPORTS

The relative merits of this form of treatment may be determined by review of the 10 cases so treated since 1940. Table 1 is an analysis of these cases.

Case 1. A well-built man, aged 28, weighing about 140 pounds, came to the hospital in March 1940, because of a swelling of the right epididymis, discovered 4 months earlier when he experienced pain upon crossing his legs. The pain was relieved under medical treatment but the swelling persisted and became associated with a weight loss of 15 pounds. Tuberculous contacts were denied. The right epididymis presented a normal head, indurated and thickened body, and a suppurating tail, pointing through the dartos. The vas was not indurated, swollen or tender. The right seminal vesicle was broad and indurated where it joined the ampulla. The prostate was indurated. There were shreds in clear urine. Rales heard at the base and apex of the right lung led to x-ray examinations which were pronounced negative. Epididymectomy and partial vasectomy permitted confirmation of the clinical diagnosis of tuberculous epididymitis. The patient was discharged on the eleventh day. Because he was advised to have the remainder of his infected genital organs removed, he returned in May for further surgery. The prostate, both seminal vesicles, the right ampulla and distal vas were removed (fig. 6); the left ampulla was sutured between the bladder neck and the membranous urethra. When the patient was discharged on the seventeenth day, he was voiding normally and his perineal wound had healed. Four months after

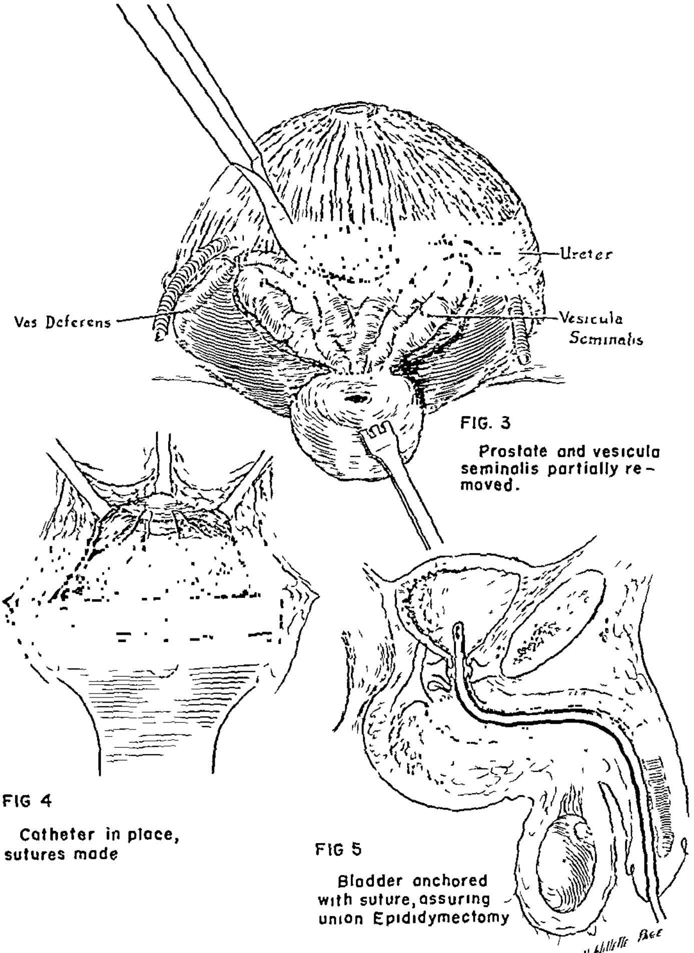


FIG. 3
Prostate and vesicula seminalis partially removed.

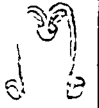
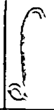
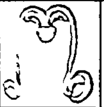
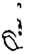
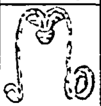
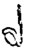
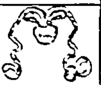
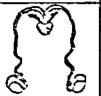
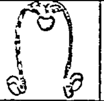
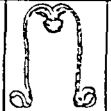
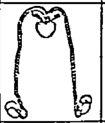
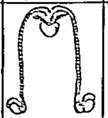
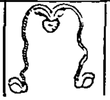
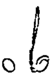
FIG 4
Catheter in place, sutures made

FIG 5
Bladder anchored with suture, assuring union Epididymectomy

FIGS. 3, 4 5

the second operation the urine was crystal clear; urethroscopy revealed the ampulla in its new location; his sex life revealed normal urges, firm erections and a satisfying climax without ejaculate, although these episodes occurred at long intervals; his general health was good. Six months postoperatively chest x-rays were negative. Though he was advised to have such examinations repeated at 6 month intervals, when he was seen again 2 years later, he had far-advanced bilateral pulmonary tuberculosis, from which he died 3 years after his first admission.

TABLE 1

Days Hospitalized	Complaint	Urinary Symp	Other Factors	Urine Test	Clinico-Surgico-Path Composite	Remaining Organs	Post Operative Course		Follow Up
							Wound	Urination	Sex life End result Morbidity
0052 Age 28 4/7 to 24/40 5/13 to 6/4/40	Painful left Scrotum 15 lbs wt loss in 4 mo.	Freq 1+	Chest ? Uro neg	2gl gl 1 shreds gl 2 clear S/C			Healed on Disc 20 Hospital days	Continent complete 11th day	Potent Died 3yrs P O Pulmonary TB 2yrs P O. Uro Neg
16798 Age 25 3/20/40 to 8/24/40	Painful swelling of right testicle for 7mo Wt loss 27 lbs	None	Chest neg Ing Lymphadenopathy Uro neg	S/C			Perineal fistula & sinuses 84 Hospital days	Continent perineal drainage	Potent 11yrs PO Perineum healed in 5mo Series of cold abscesses for 2yrs., non-spec lung abscess 5yrs PO cured - Lobectomy 9yrs PO Chest, bones, Uro neg
017517 Age 31 3/25/40 to 12/7/40	Painful, tender Perirectal & Scrotal swelling Wt loss 25 lbs	None	Chest neg Many TB sebaceous lesions Ischio-rectal abscess Uro neg	S/C			Scrotal, Inguinal, perineal, sinuses persisted 152 Hospital days	Continent freq urg tenes perineal drainage	Sex? Died 2yrs PO Wounds healed in 6mo except for loss of few drops perineally on urination Terminal Pul TB & TB enteritis Uro neg
05209 Age 23 1/28/41 to 4/8/41	Right Scrotal swelling 7mo	None	Chest neg Uro neg	S/C			Primary healing 18 Hospital days	Continent complete on disc	Potent 10yrs PO Excellent health Uro neg
021455 Age 39 2/15/42 to 3/7/42	Rectal pain & discomfort 1mo	None	Chest neg Impression ca Prostate Ascites drained 30yrs ago Uro neg	S/C			Primary healing 20 Hospital days	Continent complete 10th day	Potent 9yrs PO Excellent health Uro neg
6604 Age 28 2/15/44 to 3/25/44	Draining sinus Left Scrotum	None	Chest neg Uro neg	S/C			Healed via granulation 17 Hospital days	Continent complete on disc	Potent 7yrs PO Wound healed in 5 wks Excellent health Uro neg
15166 Age 23 5/2/45 to 6/1/45	Freq urg terminal pain & hematuria 5yrs	Freq urg tenes term hematuria	Chest neg Orchidectomy *Contralateral* Vasectomy Lt Nephrectomy for TB '41	H/C			Healed on disc. 28 Hospital days	Incontinence	Potent 6yrs PO Incontinence persisted, *tapered off to nocturnal* continence & small diurnal loss Excellent health Uro neg
18517 Age 29 8/15/45 to 10/2/45	Bilat Scrotal swellings 14mo Inguinal suppuration 4wks	None	Chest lesion controlled during 10mo sanatorium contralateral Epi involved Uro neg	S/C			Primary healing 19 Hospital days	Continent complete on disc.	Potent 5½yrs PO Good health After 3yrs non-clinical Uro TB ℞ 1grm Strep daily for 6mo Neg Uro TB
56587 Age 36 3/24/50 to 4/6/50	Low back pain	None	Chest neg Uro neg TB invaded vasa, L&R epi & left testis during period of Strep ℞	S/C			Healed via granulation 12 Hospital days	Continent perineal drainage	Potent 1yr PO No perineal leakage 20th dy, Healed 26th day Cold abscess over back yielded 400cc "Sterile pus" Spinal lesion 12L - fused 11mo PO
60017 Age 13 8/25/50 to 10/6/50	Painful Scrotal swelling 3wks	None	Chest neg Uro TB Non-clinical	C/C			Primary healing 17 Hospital days	Continent complete after 7 days	Sex? 6mo PO 1gm Strep daily and PAS effected Sterile culture in 5mo

Case 2. A man 25 years of age sought treatment in March 1940, because of a swelling in the right scrotum uncomplicated for 7 months but complicated by pain, fever, sweats and loss of weight for one month. There were no symptoms or signs referable to the urinary or other organ systems of the body. The right scrotum was the site of a hydrocele. Its evacuation revealed a testis enlarged and tender in all of its component parts. The prostate was slightly enlarged, tense and tender; the seminal vesicles were markedly enlarged and tender. The inguinal lymph nodes were palpable. Removal of the obviously tuberculous right testicle did not cause clinical improvement. Because of the belief that the brisk and persistent fever was due to an unrecognized infection outside the genital tract, valuable time was lost endeavoring to determine its nature with the aid of medical consultants. It was weeks later, after the completion of the radical surgery in case 1, that attention was focused upon the markedly enlarged seminal vesicles as the foci of infection possibly responsible for the clinical course of this patient. The perineal operation revealed marked tuberculous suppuration in the prostate as well as in the seminal vesicles These organs, with the ampullae and enveloping fasciae were removed through a perineal incision and the distal part of each vas and inguinal lymph nodes were removed through accessory inguinal incisions. The left epididymis was not disturbed. Postoperatively there was a dramatic decline of the temperature to normal by the sixth day but leakage from the perineal wound prolonged the convalescence. A follow-up study 6 months after his discharge revealed a normal chest and a satisfactory sex life, though there was a persistent scrotal sinus and a recurrent perineal fistula required urethral dilatation for its eventual cure. Two years after his discharge from the hospital the patient was readmitted for relief from a fluctuant swelling of 2 months' duration which had appeared as a painless enlargement in the right inguinal

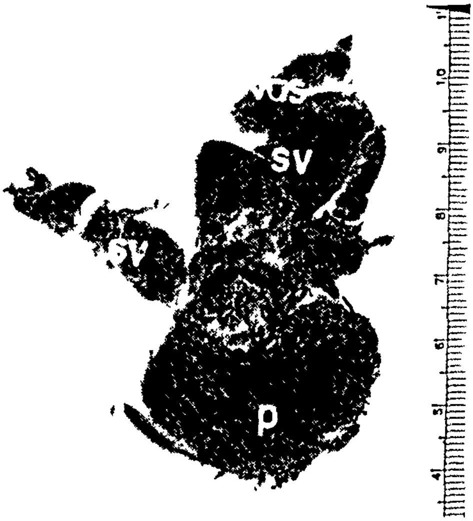


Fig. 6. Case 1. Fluctuant suppuration of right prostato-seminal vesicle area, large indurated right seminal vesicle and ampulla, also smaller left seminal vesicle.

region and had spread downward into the thigh eventually causing pain on motion and standing. There had been an attendant weight loss and a productive cough. X-ray examinations of the lungs, spinal column, pelvis and hip joints were negative. The upper and lower urinary tracts were normal. Approximately 800 cc pus were evacuated from the involved area. No organisms were found in the exudate. Irrigations of the part caused healing within 30 days. Another "cold" abscess over the sacrum caused his readmission in April 1942. The patient was last seen in April 1950, while recovering from a lobectomy for a nonspecific lung abscess. He gave an interval history of pneumonia in 1945 and a lung abscess treated in 1946 but his urinary tract had remained free from involvement, his sexual life and general health had been excellent in the intervals between his acute episodes.

Case 3. A man aged 31 was admitted to the hospital because of a tender swelling in the right ischiorectal fossa. He gave a history of a urethral discharge 3 months earlier, which had become associated with a painful swelling in the right scrotum and with a weight loss of 25 pounds. When transferred to the urologic service, the ischiorectal abscess had ruptured; the right scrotum presented a hydrocele which obscured discrete foci of suppuration in the head and body of the epididymis and a broad and indurated tail; the prostate was moderately enlarged and granular; the seminal vesicles were broadened but of normal consistency; x-ray examinations of the chest, spine and hip were negative; the urine was clear in the second glass. The right testicle, epididymis and proximal part of the vas were removed when exploration proved them to be tuberculous. Convalescence was retarded by suppurating sinuses and the development of tuberculous inguinal lymphadenitis. After catheterization of the right ejaculatory duct had proved the tuberculous nature of the infection in the prostatoseminal vesicle region, a perineal operation and secondary inguinal operations were performed with removal of the prostate, both seminal vesicles, ampullae, distal portions of each vas, and in addition, regional lymphadenopathy. His convalescence was stormy, long, and never complete. He was discharged with his operative wounds healed but for a fistula in the perineum which drained a few drops of urine on micturition, but he was admitted 6 months later with multiple swellings of the body surface which yielded tuberculous organisms. He developed clinical evidence of pulmonary disease and died two years later of pulmonary tuberculosis.

Case 4. A professional prize-fighter of 23 years noticed a swelling in his right scrotum following an injury sustained while training in a gymnasium. Medical treatment was not curative. Suppuration developed, followed by the formation of a draining sinus. The urine was clear except for a few shreds in the first glass. The lungs, lymph nodes, and bones were normal. The scrotum presented induration and a draining sinus from the tail of the right epididymis. The left testicle was normal but both vasa were indurated, the prostate was moderately enlarged and there was widening of the seminal vesicles. The right epididymis was removed. Because there was no healing, 2 months later the right testicle was removed. Subsequently the remainder of the genital tract was removed, including the left epididymis but excluding the left testis. Convalescence was uneventful. For 9½ years since the operation, the patient's health has been excellent and his sexual life satisfactory.

Case 5. A 39 year old patient sought relief from persistent rectal pain and discomfort. He had no urinary symptoms. Swelling in the left scrotum 6 months earlier, followed by swelling in the right scrotum within 5 months, had not caused discomfort. Physical examination revealed a stony hard, nodular and fixed prostate, joined at the base by broad, firm and tense seminal vesicles. The urine was clear except for shreds in the first glass. There were no clinical evidences of disease elsewhere. The prostate was explored under a presumptive diagnosis of carcinoma but frank suppuration was encountered and a biopsy confirmed the suspicion of tuberculosis aroused by the suppuration. The entire genital tract was removed with the exclusion of the two testes. Convalescence was satisfactory. The patient has been followed for more than 8 years. His health remains good and his sex life is entirely satisfactory to his mate as well as to himself.

Case 6. A 28 year old patient gave a history of recurrent attacks of painful swellings in the right and left scrotal regions over a period of 10 years. The last attack, beginning 6 months earlier, had left a firm swelling on the left side which gradually softened. Examination revealed a small but nodular prostate, nodular seminal vesicles, indurated vasa, a thickened right epididymis and an indurated left epididymis with suppuration in its tail. The testes appeared normal and the remainder of the examination revealed nothing unusual. The urine was hazy with shreds in the first glass, but the second glass was clear. At operation the left testicle was found to be involved and was removed, followed by removal of the remainder of the genital system including the right epididymis but excluding the right testis. Upon removal of the urethral catheter on the seventh day there was perineal leakage which persisted for 10 additional days. This patient, followed more than 6 years, has remained in good health and experiences a natural sexual life.

Case 7. A 29 year old patient was admitted with a fluctuant left scrotal swelling, suppuration of right inguinal lymph nodes and a tender enlargement in the right scrotum. The left scrotal swelling had appeared more than 14 months earlier as a painful complication of moderately advanced pulmonary tuberculosis. Ten months of sanatorium care arrested the pulmonary disease. The right inguinal swelling appeared during the follow-up treatment with pneumothorax refills, grew rapidly and produced pain in the back, but the pain disappeared when the swelling became fluctuant. There were no urinary symptoms and the urine was clear except for shreds in the first glass. The left scrotum contained an epididymis with indurated head and body and a suppuration in the tail. The prostate was enlarged, tender, firm, and nodular. The right epididymis had a broad, ovoid, and firm tail. The seminal vesicles were widened and indurated. Surgery was performed in two stages separated by 5 days. The first operation consisted of bilateral epididymectomy with exteriorization of the proximal vas bilaterally high in the inguinal regions and drainage of the suppurative right inguinal lymphadenitis; the second operation effected the removal of the prostate, seminal vesicles, and the remainder of the vasa. Healing was uncomplicated. Since operation the patient's sexual life has been adequate. During the summer of 1949 he felt fatigued and noted some frequency. Urologic study revealed a low grade pyuria and tuberculous bacilluria, without demonstrable evidence of active renal tuberculosis. Treatment with 1 gm. dihydrostreptomycin daily for 3 months followed by 1 gm. 3 times weekly for 3 months relieved him completely. He was well when last seen in May 1950.

Case 8. An asthenic youth of 19 years was hospitalized because of right lower quadrant abdominal pains, urinary frequency, urgency, tenesmus, terminal pain and hematuria. His father had died of pulmonary tuberculosis 4 years earlier. Nine months before admission he had been hospitalized elsewhere because of frequency and urgency. It was determined that he had clinical renal tuberculosis. Chemotherapy and local measures gave relief. Four months later he was readmitted to the same hospital with a painful and tender swelling in the right scrotum. Because he did not wish to be transferred to the tuberculosis ward, he sought admission to Freedmen's Hospital. The significant findings were: tenderness to deep palpation in the right lower abdominal quadrant; thickened and indurated right epididymis; natural right vas; prostate not enlarged but tender; palpable seminal vesicles; severely inflamed bladder with limited capacity; diminished function and x-ray evidence of tuberculosis of the left kidney; urine cloudy and acid, containing many pus cells and erythrocytes, E. coli, nonhemolytic streptococci and B. tuberculosis; negative right upper urinary tract; moderate mediastinal lymphadenopathy, especially at the left hilum but no evidence of exudative pulmonary lesions revealed by x-rays. A left nephrectomy was performed. The wound was closed without drainage but broke down. Twenty-four days later the right testicle, epididymis and part of the vas were removed. The left vas was sectioned. Convalescence was slow. Eventually the patient improved and gained weight, but the urinary symptoms persisted. Though the patient was advised to have the remainder of his infected genital tract removed, he put off this operation for 4 years until his hematuria worsened to the point that he was passing blood clots with difficulty. By that time, his prostate had become enlarged, indurated and diffusely granular, the seminal vesicles had become enlarged and indurated and the posterior urethra and the trigone of the bladder were deeply injected, but there was no evidence of active tuberculosis outside of the genital tract. The prostate, seminal vesicles and distal portions of the vasa were removed. The external sphincter was severely damaged posteriorly. Perineal leakage occurred postoperatively and incontinence became a disturbing factor but eventually healing occurred. When he was interviewed in July 1950, the patient was in good health. He had married and enjoyed a natural sexual life; he had become continent by night and was not inconvenienced by day as long as he voided at approximately 2-hour intervals.

Case 9. An obese man 36 years old suffered with low back pain for about 2 years before seeking medical aid. Treatment by an orthopedic surgeon for 6 months did not give relief. A painless swelling of the scrotum caused him to be referred for urologic study. A moderately severe prostatitis and a mass in the scrotum having the size and consistency of a testicle were found. The latter had a cord-like connection to the perineal muscles. Resection of the mass revealed a sterile abscess showing merely nonspecific inflammation of its walls. Prostatic massage and courses of treatment with penicillin and streptomycin neither reduced the quantity of the exudation in the prostatic secretion nor relieved the back pain. A mild attack of epididymitis on each side caused a second hospitalization about 6 months after the first one in order to secure biopsies of the epididymides. Suppuration was found in the tail of the left epididymis. Epididymectomies were performed. The tissues studied were reported negative for tuberculosis but re-evaluation of the biopsies 3 months later led to a diagnosis of tuberculous epididymitis. The left scrotal wound did not heal and because of a tendency of the testicle to extrude through the unhealed wound, an orchiectomy was performed. This specimen too revealed caseous tuberculosis.

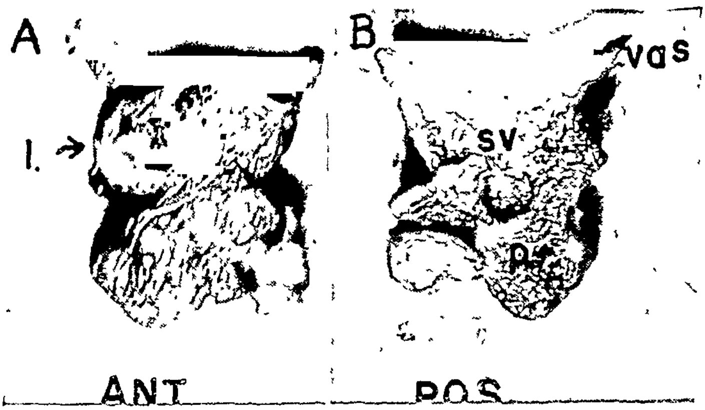


FIG. 7. Case. 9 *A*, anterior surface of prostate, ampullae and seminal vesicles. *1*, Large abscess of seminal vesicles. *B*, posterior surface of prostate, ampullae and seminal vesicles.

Radical surgery was advised. The chest and urinary tract were studied and found normal. After a course of streptomycin the radical operation was performed, but with some misgivings because of the absence of positive findings on rectal examination. However, at operation, pus was found in the prostate and in the seminal vesicles; the ampullae and vasa were found engorged and swollen (fig. 7). These structures were removed, but in the course of their removal the vesicles were ruptured. The perineal wound was closed with drainage. Urine was passed through the perineal wound for about 5 weeks after the operation. While convalescing and while under streptomycin therapy, the patient experienced pain and developed tenderness in the right lumbar region. A mass was found at this site which persisted after the subsidence of the symptoms. About 400 cc of sterile purulent material was removed; drainage was established and the site healed. Urinary continence and normal sex relations are known to exist.

Case 10. A 13 year-old boy was admitted to the hospital in August 1950, because of a swelling of the scrotum. It had started 3 months earlier with pain. The pain subsided within a week, but the swelling persisted, became soft about 1 week prior to admission, and ruptured spontaneously. Tuberculous contacts were denied. Careful examination, including x-rays, ruled out the presence of pulmonary and renal tuberculosis. The only significant findings were: enlargement of the left epididymis with two sinuses draining from the tail; nodular induration of the left vas; enlargement of the base of the left seminal vesicle with a suggestion of fluctuation and slight induration of the left prostatic lobe. Though the urine was cloudy in both glasses, it did not yield tubercle bacilli by culture. On September 7, 1950, the left epididymis was removed and the vas exteriorized through an inguinal incision. Twelve days later, perineal prostatectomy, bilateral seminal vesiculectomy, complete left vasectomy and partial right vasectomy were performed. The operative wounds were healed when the patient was discharged on the seventeenth day after the radical operation. Urine studies five months postoperatively were normal and the patient was in good health, although under a course of streptomycin therapy.

SUMMARY AND CONCLUSIONS

A critical appraisal of the factual data and authoritative opinions available in 1940 on the pathogenesis and treatment of genital tuberculosis in the male led to beliefs and conclusions at variance with those generally accepted at that time. The available evidence did not appear to support the belief that, in the absence of clinically demonstrable renal tuberculosis, genital tuberculosis in the male is due to a hematogenous implantation, usually in the epididymis. The evidence did appear to support the premise that the infection results from subclinical renal tuberculosis, with involvement of the genital tract beginning in the prostate and seminal vesicles with secondary spread by way of the vasa to the epididymis.

This premise rendered untenable any form of surgical treatment of tuberculous epididymitis which did not take into account the parent lesions in the prostate and seminal vesicles. Accordingly, conservative forms of surgical treatment were abandoned in favor of radical measures for patients with tuberculosis limited to the genital organs or with tuberculosis of other organs under control. This form of treatment has as its object the removal of the obvious disease in either epididymis, as well as the less obvious disease in the corresponding vas, both seminal vesicles and prostate, and the ligation of the vas on the nondiseased side in unilateral cases.

The experience with this form of treatment in 10 patients over a period of nearly 11 years has been reviewed. The results warrant the belief that the premise adopted in 1940 was sound and the form of treatment evolved was justified.

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MULTICENTRIC ORIGIN OF PAPILLARY TUMORS OF THE URINARY TRACT

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That many neoplastic diseases are of multiple origin is fairly generally accepted. Such lesions as the lymphomas, chloromas, multiple myelomas, certain types of carcinoma of the liver, multiple carcinoma of the bowel and neurogenic sarcoma commonly occur as multiple tumors. In this investigation, an attempt has been made to determine whether or not multiple papillary epitheliomas in the urinary tract originate from multiple foci in the epithelial lining of the urinary passages. It is difficult to determine this from a histologic standpoint because by the time most lesions produce clinical findings they have obliterated all trace of their origin. This is a study of the chronologic development and location of multiple papillary tumors in the urinary tract and is presented in an attempt to clarify the question. The important historic background has been reviewed as have also the other concepts that have been offered to explain the origin of multiple papillary tumors in the urinary tract.

MATERIALS AND METHOD OF STUDY

The material for this study was obtained from two sources: the clinical records and the specimens of surgically removed tissue of cases of tumors of the renal pelvis at the Mayo Clinic during the years 1911 to 1947, inclusive. Cases were excluded if tissue was not available. Tumors of the renal pelvis were selected as a basis for this study because they are frequently accompanied by similar tumors of the ureter and bladder.

The records were carefully studied for pertinent chronologic data in the development of multiple neoplasms in the urinary tract. The location of neoplasms in the bladder that appeared synchronously or asynchronously with similar growths in the renal pelvis and ureter was designated in most instances in the cystoscopic report.

The sections of tissue were studied under the microscope and classified according to the following three types: 1) papillary epitheliomas without evidence of infiltration of the subjacent wall, 2) papillary epitheliomas with infiltration and 3) nonpapillary infiltrating epitheliomas. This classification has been described previously by McDonald and Priestley. Tumors of the first type were

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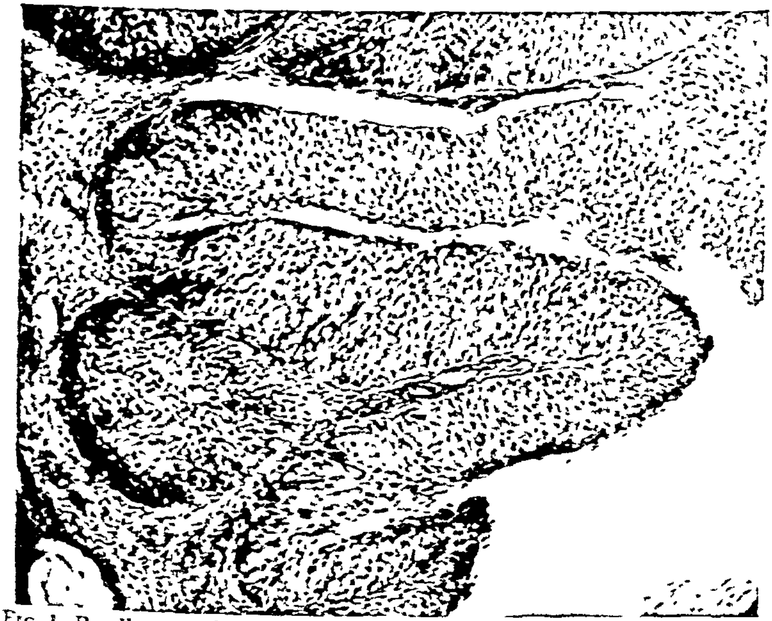


FIG. 1. Papillary epithelioma of renal pelvis. hematoxylin and eosin; ×8

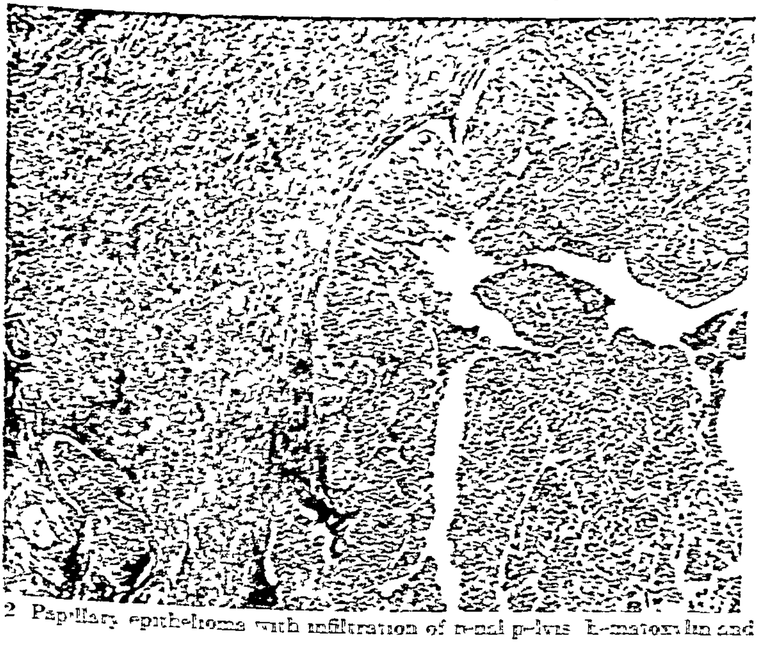


FIG. 2. Papillary epithelioma with infiltration of renal pelvis. hematoxylin and eosin. ×[illegible].

characterized by villous fronds which projected into the lumen of the renal pelvis, ureter or bladder. Histologic evidence of infiltration into the wall beyond the basal cell layer of the lining epithelium was not present (fig. 1). This type included lesions of grade 1 (Broders' classification), considered by many pathologists as benign papillomas. The second type of tumors, designated as papillary epitheliomas with infiltration, was similar to the first type except that infiltration had taken place into the muscle of the pelvis of the kidney, the peripelvic tissue or the parenchyma of the kidney and analogous structures in the ureter and bladder were involved (fig. 2). The third type, the nonpapillary epitheliomas, included tumors that had infiltrated to varying degrees beyond the depth of the lining epithelium of the renal pelvis, ureter and bladder (fig. 3). Single neoplasms were included in this study for the purpose of comparison of statistical data with similar data for the multiple group.

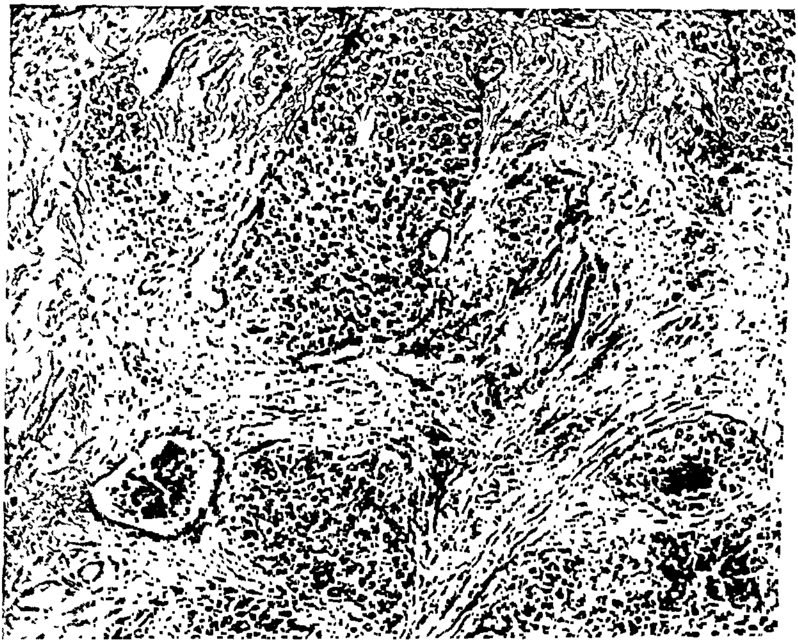


FIG. 3. Nonpapillary infiltrative epithelioma of renal pelvis (hematoxylin and eosin; ×100).

A discussion of the signs, symptoms, associated pathology and laboratory findings is not applicable in this study and was therefore not included. Part of the material used has been reported by Scholl, Foulds, Scholl and Braasch, Hunt, Hunt and Hager, Cabot and Allen and McDonald and Priestley.

HISTORICAL BACKGROUND

Little was known about tumors of the renal pelvis prior to 1900. The study of the disease was confined to findings at necropsy and to reports of isolated cases in the literature. The earliest reference to primary tumors of the renal pelvis appears to have been made by Rayer in 1840. He described a case in which the mucosa of the renal pelvis was studded with 7 red polypoid excrescences. A similar polyp was found in the upper portion of the ureter. Murchison, in 1870, described a case of villous disease of the kidneys and bladder. In a summary of the findings at necropsy the growths were described as villous processes arising from the mucous lining of the pelvis of each kidney and present also at the base of the bladder surrounding both ureteral orifices. This appears to be the first recorded case of bilateral tumors of the renal pelvis and in each of the cases just mentioned the tendency toward multiple involvement of villous tumors in the urinary tract was noted.

Four theories have been advanced to account for the multiplicity of papillary tumors in the urinary tract; namely, 1) the theory of implantation, 2) the theory of multicentric origin, 3) the theory that tumors spread by direct extension along mucous membranes and 4) the theory that tumors spread by metastases by way of the lymph vessels.

Albarran and Imbert, in a review of the literature up to 1903, were able to collect only 42 cases of tumors of the renal pelvis. They divided the tumors into three groups: papillomas, papillary epitheliomas and epidermoid carcinomas (nonpapillary).

In the group designated as papillomas they reported that the incidence of involvement of ureters and bladder by similar growths was high. They expressed the opinion that involvement of the ureters and bladder was the result of an implantation of neoplastic cells which had exfoliated from the primary tumor in the renal pelvis. These cells were carried in the urinary stream and deposited as graft implants on the lining epithelium of the ureter, bladder or both. Savory and Nash, Judd, Scholl, Young, Joly, Kimball and Ferris, and more recently Macalpine have supported this concept of implantation to account for multiple papillary tumors in the ureter and bladder associated with similar tumors in the renal pelvis.

Hansemann, in 1890, first introduced the concept of the multicentric origin of tumors. He expressed the opinion that new independent foci develop in the neighborhood of the original tumor and the subsequent coalescence of these foci results in extension of the tumor. Ewing stated that neoplastic cells may originate from several centers, that they may appear simultaneously or at intervals and they may either coalesce or remain discrete. In discussing papillary tumors of the urinary tract he stated that multiplicity was more often the result of factors affecting the entire mucous membrane rather than implants as described by Albarran and Imbert. Morogna, Fowler, Caulk, Johnson, McDonald and Priestley and Slaughter also expressed the opinion that the presence of multiple papillary tumors in the urinary tract could be explained best on the basis of multicentric origin.

Hunt, in 1929, stated that papillary epitheliomas of the renal pelvis metastasized to the mucosa which lined the urinary passages if sufficient time had elapsed.

Stevens, in 1920, reported a case of papilloma of the renal pelvis that developed 1½ years after excision and fulguration of a similar tumor in the bladder. The vesical neoplasm was located "to the left of the left ureteral orifice" and the right kidney was involved. He expressed the opinion that the tumor of the kidney was secondary to the primary lesion in the bladder which had metastasized by way of the lymphatic stream.

Garceau, in 1909, stated that papillomas of the renal pelvis were to be regarded as benign tumors with decided tendencies toward malignant disease and capable of metastasizing to the ureter and bladder.

Haessler, in 1921, reported a similar case and also expressed the opinion that the primary tumor in the bladder had metastasized by way of the lymphatic channels to the kidney.

The four theories that have been offered to explain the multiplicity of papillary tumors of the urinary tract have each been supported by conjecture. Each author has expressed an opinion that seemed most logical to him but, unfortunately, has not had further evidence with which to support his conclusion.

In each of the many papers dealing with tumors of the renal pelvis, mention is made of the fact that similar tumors may also be found in the ureter and bladder. In most instances the cases reported have been collected from many sources and, as a result of the differences in classification, the recorded incidence of occurrence of multiple papillary lesions in the urinary tract differs with each author.

The authors who have differentiated the papillary tumors of the renal pelvis from the nonpapillary lesions reported a more uniform incidence of multiple papillary tumors in the urinary tract, about 45 per cent. They have shown that multiplicity is a characteristic of the papillary lesion.

RESULTS

Among the patients who received surgical treatment at the clinic for carcinoma of the renal pelvis during 1911 to 1947, inclusive, 133 cases were found suitable for our study.

The group of 133 cases consisted of 88 cases of single tumor of the renal pelvis and 45 cases of multiple papillary tumors involving the renal pelvis or the ureter or the bladder or all three, synchronously or asynchronously. The 88 cases of single tumor of the renal pelvis were used for the purpose of comparing statistical data. The 45 cases of multiple papillary tumors were subdivided into 3 groups—the synchronous, the asynchronous and the synchronous-asynchronous—on the basis of the time factor involved in their development. The synchronous group consisted of 18 cases in which more than one neoplasm was found in the urinary tract when the first operation was carried out. In this group new growths did not develop in the bladder subsequently. The asynchronous group consisted of 16 cases in which one neoplasm was found in the urinary tract when the first operation was carried out but new growths developed subsequently. In 5 of these cases a papillary neoplasm of the bladder preceded the development of a similar tumor in the renal pelvis. The synchronous-asynchronous group consisted of 11 cases in which more than one neoplasm was found in the urinary tract when the first operation was carried out and subsequent new growths developed in the bladder.

Sex. The incidence according to sex is presented in table 1. Seventy-five per cent of the patients having a single lesion were men and 25 per cent were women. The preponderance of men is increased in the multiple group in which 82.2 per cent were men and 17.8 per cent were women. The disparity between the sexes was uniform in the three subdivisions of the multiple group, there being a 4 to 1 preponderance of men to women.

Age. The age was recorded for each patient with a single lesion or a synchronous group of lesions at the time of treatment. The ages of patients with asynchronous lesions and synchronous-asynchronous lesions, were recorded at the time the second lesion was treated. These were used in setting up the distribution of ages by decades and in obtaining the mean age, because it was the second lesion which caused such cases to be classified into asynchronous and synchronous-asynchronous groups.

TABLE 1. *Incidence of papillary tumors of the urinary tract according to sex*

SEX	SINGLE LESION		MULTIPLE LESIONS			TOTAL CASES	PER CENT
	Cases	Per cent	Synchronous	Asynchronous	Synchronous-asynchronous		
Male	66	75	15	13	9	37	82.2
Female	22	25	3	3	2	8	17.8
Total	88	100	18	16	11	45	100

TABLE 2. *Age distribution: Single and multiple lesions*

AGE, YR	SINGLE LESION		MULTIPLE LESIONS			TOTAL CASES	PER CENT
	Cases	Per cent	Synchronous	Asynchronous	Synchronous asynchronous		
20-29	2	2.3					
30-39	1	1.2	1	1		2	4.4
40-49	12	13.6	2		3	5	11.1
50-59	31	35.2	6	8	4	18	40.0
60-69	33	37.5	9	5	3	17	37.8
70-79	9	10.2		2	1	3	6.7
Mean age	57.8		56.1	58.8	55.5		
Youngest	25		34	38	41		
Oldest	79		69	72	72		

The mean age for the group of patients with a single lesion was 57.8 years as compared to the group of patients with multiple lesions which was 56.8 years (table 2).

INCIDENCE OF TYPES OF TUMORS

The tumors were classified, as previously described, into 3 groups, papillary, papillary with infiltration and nonpapillary with infiltration. In the 133 cases studied, the papillary lesions appeared in 53 cases (39.9 per cent) and the papillary lesions with infiltration in 54 cases (40.6 per cent). The nonpapillary infiltrative lesions were present in 26 cases (19.5 per cent). In the 53 cases of papillary tumors, 58.5 per cent of the lesions appeared as multiple lesions and 41.5 per cent appeared as single lesions. In the 54 cases of papillary infiltrative tumors 25.9 per cent of the lesions appeared as multiple lesions and 74.1 per cent appeared as single lesions. In the 26 cases of nonpapillary infiltrative tumors, the lesions were present only as single lesions.

A further breakdown of the incidence of each type of lesion found in the single group as compared to the multiple group is shown in table 3. In the group of single tumors, 25 per cent of the lesions were papillary, 45.6 per cent papillary with infiltration and 29.5 per cent nonpapillary with infiltration. In the group of multiple tumors, 68.9 per cent of the lesions were papillary and 31.1 per cent were papillary with infiltration. Involvement of the urinary tract by multiple tumors appears to be a disease characteristic of papillary and papillary infiltrative lesions.

TABLE 3. *Classification of tumors of the renal pelvis of 133 cases; single and multiple lesions*

TYPE OF LESION	MULTIPLE LESIONS		SINGLE LESION		TOTAL CASES	PER CENT*
	Cases	Per cent*	Cases	Per cent*		
Papillary	31	68.9	22	25.0	53	39.9
Papillary with infiltration	14	31.1	40	45.6	54	40.6
Nonpapillary with infiltration	0	0	26	29.5	26	19.5

* Per cent of 133 cases of tumor of renal pelvis.

MULTIPLE LESIONS

Location. The 29 cases in the synchronous and synchronous-asynchronous groups were combined in the study of the location of the multiple lesions in the urinary tract that were present simultaneously. Figure 4 illustrates the segmental distribution of the multiple lesions in the group in which the renal pelvis and ureter were involved, the group in which the renal pelvis and bladder were involved and the group in which the renal pelvis, ureter and bladder were involved. Further study of the location of the lesions in these designated groups shows that the ureter was involved in 44.8 per cent of the cases. The lesions were situated in the upper portion of the ureter in 5 cases, in the lower portion in 5 cases and distributed throughout the entire ureter in 3 cases. The bladder was involved in 31.1 per cent of the cases; the lesions were situated ipsilaterally in relation to the tumor in the renal pelvis in 6 cases and contralaterally in 2 cases. In 1 case lesions occupied the entire bladder. The ureter and bladder were involved in 24.1 per cent of the cases. The lower portion of the ureter was involved in 3 cases and the entire ureter in 4 cases. The bladder was involved ipsilaterally in 6 cases and contralaterally in 1. Although lesions which involve the ureter are most frequently located at the anatomic points of narrowing and lesions which involve the bladder are most frequently located ipsilateral to the tumor in the renal pelvis, the epithelium of the entire urinary tract may be a site of neoplastic involvement.

The location of the second lesion in the bladder in relation to the tumor of the renal pelvis in 22 cases of the asynchronous and synchronous-asynchronous groups was studied also. The 5 cases in which the vesical tumor preceded the tumor of the renal pelvis were not included in this study. It was found, however,

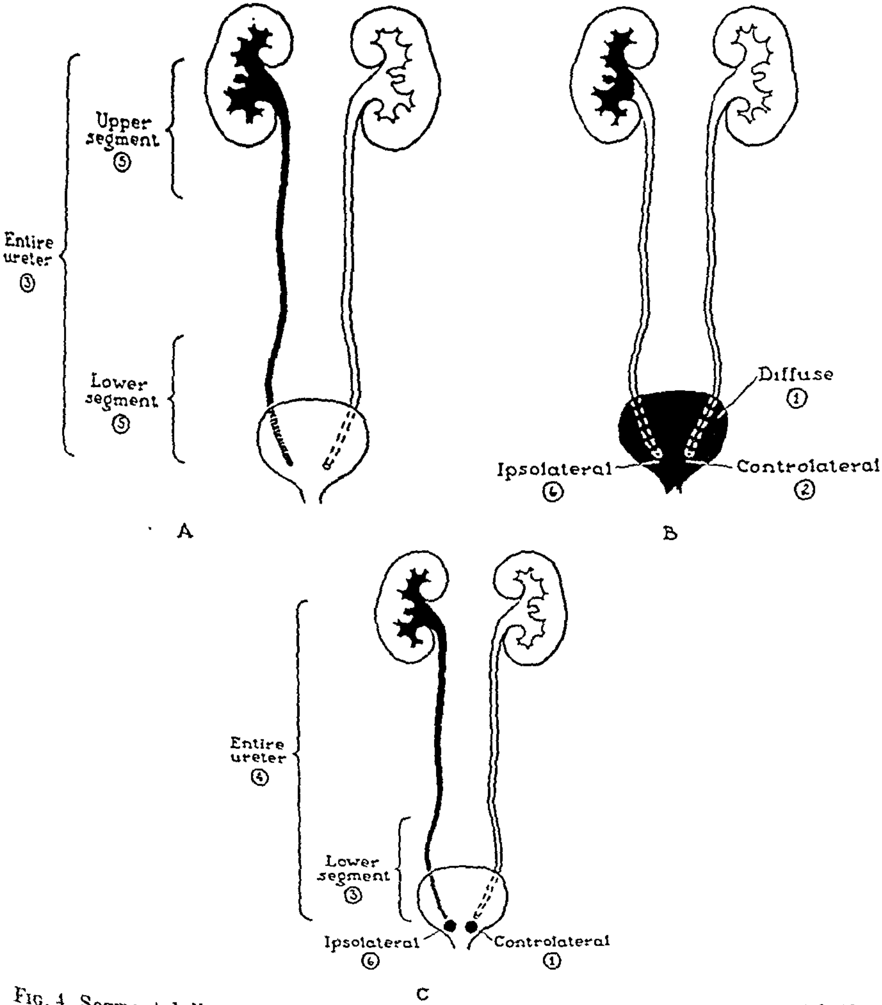
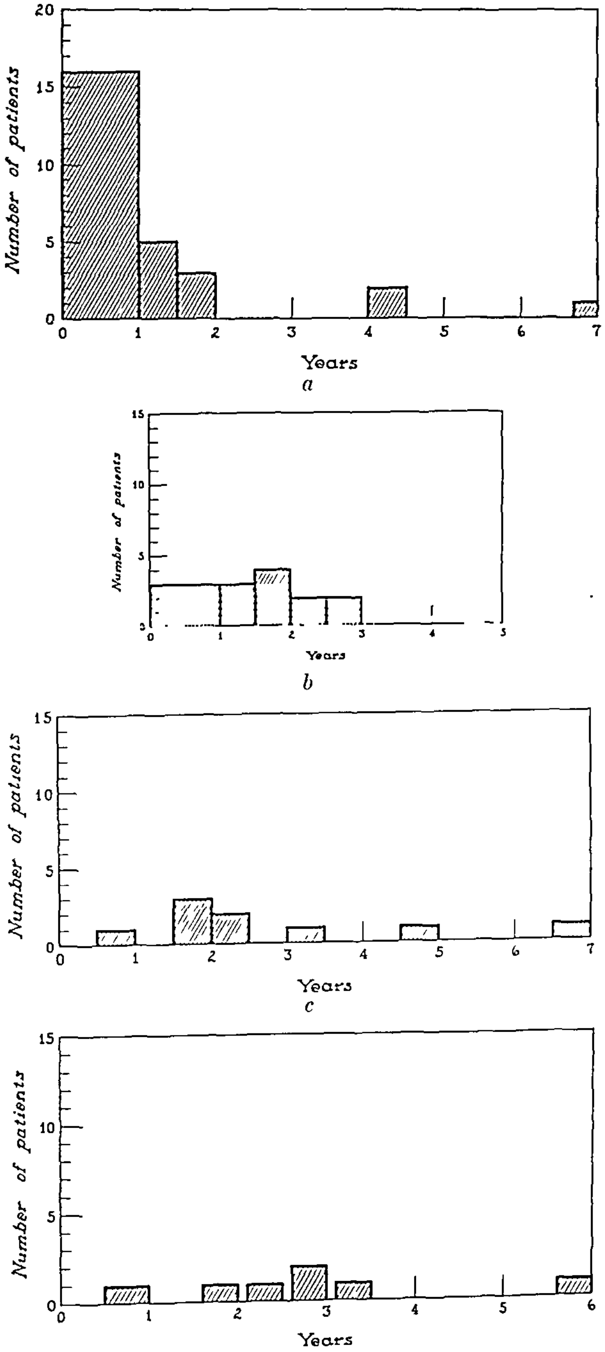


FIG. 4. Segmental distribution of multiple papillary and papillary infiltrative epitheliomas in ureter and bladder associated with similar tumors of renal pelvis. *a*, Tumors of renal pelvis and ureter; *b*, tumors of renal pelvis and bladder; *c*, tumors of renal pelvis, ureter and bladder.

TABLE 4. *Number of lesions developed in the asynchronous and synchronous-asynchronous groups*

LESIONS, NUMBER	ASYNCHRONOUS LESIONS, CASES	SYNCHRONOUS-ASYNCHRONOUS LESIONS, CASES	TOTAL CASES	PER CENT
2	5	8	13	48.2
3	4	1	5	18.5
4	2		2	7.4
5		2	2	7.4
6	1		1	3.7
8	2		2	7.4
13	1		1	3.7
25	1		1	3.7



a

b

c

d

FIG. 5 *a*, Representation of interval of time between development of first and second lesions in group of 27 patients with 2 or more lesions which developed asynchronously; *b*, interval of time between development of second and third lesions in group of 14 patients with 3 or more asynchronous lesions; *c*, interval of time between development of third and fourth lesions in group of 9 patients with 4 or more asynchronous lesions; *d*, interval of time between development of fourth and fifth lesions in group of 7 patients with 5 or more asynchronous lesions.

that the ipsilateral side of the vesical wall was involved in 54.5 per cent of the cases, the contralateral side in 13.6 per cent and the lesion was located in the dome, trigone, base, or posterior wall in 31.9 per cent of the cases. This again points out the fact that the epithelium of the entire urinary tract is a vulnerable site for tumors.

Number developed. Table 4 shows the number of lesions which developed in 27 cases in the asynchronous groups, after the removal of the first neoplasm or group of neoplasms. It is seen that in 48.1 per cent of the cases a second lesion developed, in 18.9 per cent 3 lesions developed, in 7.4 per cent 4 lesions developed and in a similar percentage 5 lesions developed. In 1 case 24 lesions developed after removal of the first group of neoplasms.

Interval of time between development. The interval of time between the removal of the first neoplasm or group of neoplasms and the development of subsequent lesions is graphically illustrated in figure 5. In the 27 cases in the asynchronous and synchronous-asynchronous groups, a second neoplasm appeared within five to twelve months in 59.2 per cent of the cases, within thirteen to eighteen months in 18.5 per cent of the cases and within nineteen to twenty-four months in 11 per cent of the cases. In 2 cases the second lesion appeared four and a half years and seven and a half years respectively, after the removal of the first neoplasm.

The intervals of time between the development of the second and third lesions, third and fourth lesions and fourth and fifth lesions also are illustrated graphically in figure 5. It is evident that there is no regularity in the space of time between the reappearance of new growths.

COMMENT

The results of our study augment the concept of multicentric origin of papillary tumors of the ureter and bladder associated with similar tumors of the renal pelvis. The criteria of Warren and Gates for multiple primary tumors, that is, "each tumor must present a definite picture of malignancy, each must be distinct and the probability of one being a metastasis of the other must be excluded," were fulfilled by the multiple papillary tumors of the urinary tract in our study. Although the histologic appearance of some papillary tumors without infiltration does not present a definite picture of malignant disease, the clinical course of many of these same lesions does. Each lesion was distinct and was separated from neighboring lesions by normal epithelium. In cases of multiple tumors the probability that one lesion was a metastatic process of another, metastasis having taken place by way of the lymph, the blood or by direct extension, has also been considered but does not seem likely in view of the following facts: In the group of 26 cases of nonpapillary infiltrative tumors examined in our study the perineural lymph vessels and the blood vessels were frequently involved, yet there were no instances of ureteral or vesical metastasis. In the 53 cases of papillary tumors there were no instances of demonstrable lymphatic or venous involvement; however, in 59 per cent of these cases there were multiple tumors which involved the ureter, the bladder, or both. This would seem therefore to exclude the lymphatics as a pathway for the spread to the ureter and bladder of papillary tumors of the renal pelvis. Presman and Ehrlich showed that metastatic lesions of the ureter involved all layers of this structure except the mucosa. As a rule, metastatic lesions of the bowel and bronchi also are situated beneath an intact mucosa. In each case of multiple papillary epithelioma studied the mucosa was involved thereby suggesting that the tumors arose from the mucosa and not from metastasis by way of the lymph or blood. The normal intervening epithelium that separated the multiple lesions would seem to deny the possibility of spread by direct extension.

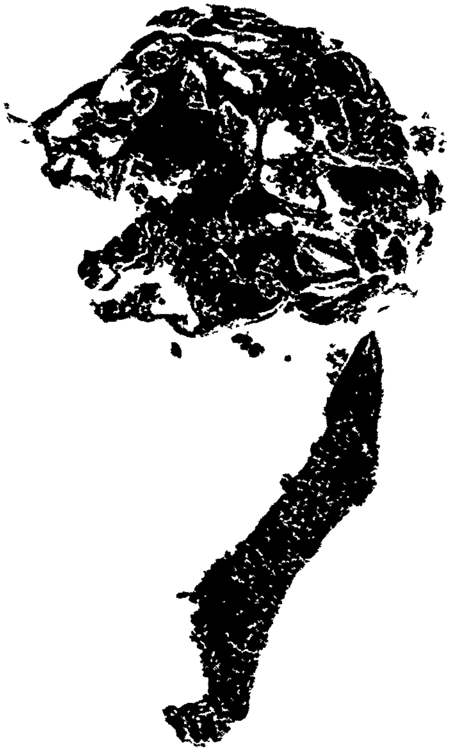


FIG. 6. Papillary infiltrative epithelioma of renal pelvis and entire ureter.

The wide range of location of the multiple papillary tumors examined in our study would seem to support further the possibility that each lesion arises from an independent focus. The papillary tumors of the ureter that accompanied similar growths in the renal pelvis were frequently located in the upper and lower segments but in several cases the entire ureter was involved (fig. 6). In the bladder, the multiple papillary growths were most often found ipsilateral to the tumor in the renal pelvis but other areas in the bladder were also the sites of multiple growths. Although papillary epitheliomas involving the urinary tract bilaterally are rare, when this condition is present it can best be explained on the basis of multicentric origin.

The pattern of growth of multiple papillary tumors paralleled the direction of flow of urine from the renal pelvis to the bladder, that is, the initial lesion developed in the renal pelvis and subsequent new growths developed in the ureter, the bladder or both. In 5 cases a papillary tumor of the bladder preceded the appearance of a similar growth in the renal pelvis. This order of events further supports the concept of the multicentric origin of multiple papillary tumors of the urinary tract.

The removal of the initial lesion or group of lesions does not preclude the possibility of the development of new growths in the remaining portions of the urinary tract. In our study asynchronous new growths developed in 25.2 per cent of the 107 cases of papillary and papillary infiltrative tumors. In the majority of cases 2 lesions developed but in several cases from 3 to 25 new growths developed. The interval of time between the removal of the initial lesion and the development of new growths is variable. The majority of recurrent new growths developed within one year after the removal of the initial lesion but in several instances the time varied from two to seven years. It does not seem probable that epithelial cells which have exfoliated from a parent tumor and have been bathed in urine for a variable time can become embedded and grow on intact epithelium. From the foregoing evidence it seems plausible to postulate that the factors responsible for the development of the initial lesion may continue to provide the necessary impetus for the development of new tumors in the remaining portion of the urinary tract.

The multiple tumors in the group studied were histologically either papillary or papillary with infiltration. Multiplicity of tumors did not occur in the nonpapillary infiltrative group of lesions. This obvious difference in the papillary lesions as compared to the nonpapillary would seem to indicate a difference based on etiology since the papillary as well as the nonpapillary lesion possesses the potentiality of metastasis or exfoliation. According to Broders, in the majority of cases of multiple and recurrent tumors of the urinary tract, the uniformity of the histologic change can be compared with that of adenomas or polyps of the large intestine. When these polyps undergo carcinomatous transformation, they are independent of each other and present a uniform histopathologic picture. Broders also said that papillary growths of the renal pelvis, ureter and bladder show a definite continuity with the basal cells of the mucosa and that this indicates that the tumors originate in these cells.

It is difficult to prove from a histologic standpoint that multiple papillary tumors of the urinary tract are multicentric in origin because by the time most lesions produce clinical findings, they have obliterated all trace of their origin. A logical evaluation of the location, chronologic development and the histologic characteristics of multiple papillary tumors of the urinary tract, however, augments the concept that these tumors are of multicentric origin.

SUMMARY AND CONCLUSIONS

The incidence of multiple papillary tumors in the ureter and bladder associated with similar tumors in the renal pelvis varied with the type of lesion. In 58.5 per cent of 53 cases of papillary epithelioma of the renal pelvis, either synchronous or asynchronous papillary lesions occurred in the ureter, the bladder or both. In 25.9 per cent of 54 cases of papillary infiltrative epithelioma of the renal pelvis a similar lesion occurred in the ureter, the bladder or both. There were no cases of multiple involvement in the nonpapillary group.

It was found that the epithelium of the entire urinary tract might be the site of involvement of multiple papillary tumors. Study showed the interval of time between the development of new growths to be variable. The development of multiple papillary tumors was not dependent on the presence of a parent tumor. These tumors probably originate from multiple independent foci.

All patients with papillary tumors of the urinary tract should have frequent re-examination. The destruction or removal of multicentric epitheliomas does not eliminate the predisposition for similar growths to recur.

REFERENCES

Albarran, Joaquin and Imbert, L.: Les tumeurs du rein. Paris: Masson et Cie, 1903, pp 452–459.

Broders, A. C.: Discussion, Proc. Staff Meet., Mayo Clin., **13**: 499–500, 1938.

Cabot, H. and Allen, R. B.: Epithelioma primary in the renal pelvis: Report of forty-five cases. Lancet, **2**: 1301–1306, 1933.

Caulk, J. R.: Tumors of the renal pelvis and ureter. Trans. Am. A. Genito-Urin. Surg., **30**: 51–62, 1937.

Ewing, J.: Neoplastic Diseases; a Treatise on Tumors. Ed. 3, Philadelphia: W. B. Saunders Company, 1928, pp. 36, 806, 908, 912.

Foulds, G. S., Scholl, A. J. and Braasch, W. F.: A study of histology and mortality in renal tumors. S. Clin. North America, **4**: 407–424, 1924.

Fowler, H. A.: Solitary papilloma of lower ureter (right) secondary to recurrent papillomata of the bladder. J. Urol., **27**: 561–580, 1932.

Garceau, E.: Renal, Ureteral, Perirenal and Adrenal Tumors, and Actinomycosis and Echinococcus of the Kidney. New York: D. Appleton-Century Co., Inc., 1909, 421 pp.

Haessler, F. H.: Papillary epithelioma of bladder, metastatic in kidney. J. A. M. A., **76**: 446–447, 1921.

Hansemann, David: Ueber asymetrische Zelltheilung in Epithelkrebsan und deren biologische Bedeutung, Virchows Arch. f. path. Anat., **119**: 299–326, 1890.

Hunt, V. C.: Method of metastasis of papillary epithelioma of the renal pelvis. S. Clin. North Amer., **9**: 853–861, 1929.

Hunt, V. C. and Hager, B. H.: Review of 271 cases of malignant renal neoplasms. S. Clin. North Amer., **9**: 149–159, 1929.

Johnson, F. P.: Papillary tumors of the kidney pelvis. Northwest Med., **38**: 236–240, 1939.

Joly: Quoted by Caulk.

Judd, E. S.: Papillary tumors of the pelvis of the kidney. Journal-Lancet, **39**: 247–253, 1919.

Kimball, F. N. and Ferris, H. W.: Papillomatous tumor of the renal pelvis associated with similar tumors of the ureter and bladder. Review of literature and report of two cases. J. Urol., **31**: 257–304, 1934.

McDonald, J. R. and Priestley, J. T.: Carcinoma of renal pelvis: Histopathologic study of seventy-five cases with special reference to prognosis. J. Urol., **51**: 245–258, 1944.

Macalpine, J. B.: Papillomatous disease of the renal pelvis. Brit. J. Surg., **35**: 113–132, 1947.

Morogna, P.: Quoted by Judd, E. S.

Murchison, C.: Case of villous disease of the bladder and kidneys. Tr. Path. Soc. London, **21**: 241–244, 1870.

Presman, D. and Ehrlich, L.: Metastatic tumors of the ureter. J. Urol., **59**: 312–325, 1948.

Rayer: Quoted by Savory and Nash.

Savory, H. and Nash, W. G.: Benign villous tumour of the renal pelvis; haemothorax; nephrectomy; recovery. Lancet, **2**: 1699–1702, 1904.

Scholl, A. J.: Papillary tumors of renal pelvis. Surg., Gynec. & Obst., **38**: 186–199, 1924.

Slaughter, D. P.: Multiplicity of origin of malignant tumors; collective review. Internat. Abstr. Surg., **79**: 89–98, 1944.

Stevens, W. E.: Tumors of the renal pelvis. J. A. M. A., **74**: 1576–1577, 1920.

Warren, S. and Gates, O.: Multiple primary malignant tumors; a survey of the literature and a statistical study. Am. J. Cancer, **16**: 1358–1414, 1932.

Young, H. H.: Discussion. Brit. J. Urol., **5**: 338–339, 1933.

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FLUID BALANCE IN THE UROLOGICAL PATIENT: DISTURBANCES IN THE RENAL REGULATION OF THE EXCRETION OF WATER AND SODIUM SALTS FOLLOWING DECOMPRESSION OF THE URINARY BLADDER

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The removal of an obstruction in the lower urinary tract is followed ultimately by a reversal of the disturbances of renal function attendant upon the obstruction, provided that the individual survives the decompression and the inherent functional capacity of the kidneys has not been lost.

In general, it is assumed that the process of recovery of renal function following the removal of the cause of the strangury is orderly in the physiologic sense. That is to say, from the moment of decompression all components of renal function begin to recover in such a manner as to foster the recovery of health.

Certain gross clinical observations made during the past decade have led to the belief that this therapeutic thesis is not always true. In other words, the observation that decompression of the bladder occasionally increased the gravity of illness led to the concept that relief of the urinary obstruction brought on renal functional abnormalities that might be more immediately dangerous to life than those existing before the obstruction was relieved.

The physiologic changes occasionally attending decompression of the bladder are only rarely attended by chills, since the introduction of potent antibiotics. These post-decompressional physiologic changes are now most often characterized by the development of oligemia, the loss of cutaneous elasticity, and the onset of progressive weakness, anorexia, depression of the central nervous system, and peripheral circulatory failure. These are signs of a deficiency of extracellular fluid. Since they have been seen to develop while no vomiting, meteorism, sweating, or diarrhea existed, the kidneys were naturally suspected as the route whereby the sodium salts left the body in excessive amounts.

CASE SUMMARIES

Case 1—(A. F., No. 66068) and case 2—(R. H. No. 59521) are representative of early clinical experience with the aggravation of fluid imbalance by decompression of the bladder before facilities for the easy performance of sodium analyses of urine and serum were available.

Figures 1 and 2 show graphically their daily exchanges of water following catheterization. The sodium exchanges could not be established in these cases because the urinary losses of sodium were not determined. The rate of loss of chloride in urine for a number of days was known in both instances but the sodium losses cannot be calculated from the chloride data because more or less chloride than sodium may be lost. However, it is clear that an enormous urinary excretion of water took place soon after catheterization; R. H. (case 2) actually

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lost 15 per cent of his body water within 21 hours and A. F. (case 1) lost at least 10 per cent of it in 14 hours. If these losses of water represented the retention thereof while the urinary obstruction was present, then the loss of this fluid should have made the patient feel better or at least it should have left him feeling as well as he did before he lost it. Such was not the case because both men became worse and showed signs of a generalized insufficiency of sodium salts and water. Therefore one is led to the assumption that the kidneys of these men did not immediately regain their water and salt conservation capacities following decompression. In fact, A. F. (fig. 1) had not regained much water regulating capacity for 4½ days; his excretion of urine consistently exceeded the sum of the fluid he ingested and that provided by oxidation for the above period of time. R. H. (fig. 2) stopped the excessive excretion of water by the end of 21 hours and after the elapse of 45 hours his kidneys were regaining their capacity for saving water as shown by the decrease in the cumulative negative balance for water after that time.

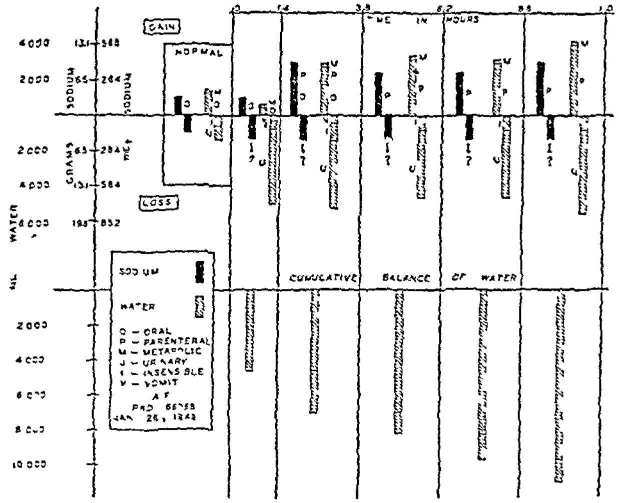

FIG. 1. Case A. F. (No. 66068). Ordinates of graphs 1, 2, 3 and 4 are so arranged that sodium segments are related to water segments as sodium of serum is related to water of serum. Sodium segment is expressed in grams and milliequivalents of sodium ion. Grams or milliequivalents of sodium expressed as sodium chloride can be obtained from these graphs by multiplying grams or milliequivalents of sodium by factor 2.52. Time is reckoned from catheterization.

Bars extending above abscissae represent intakes and bars extending below abscissae represent losses.

Normal exchange rates of water and sodium are shown in circumscribed segment on left of figures 1, 2 and 3.

Components of the exchanges in A. F. that were measured are oral and parenteral intakes of sodium salts and water. Water available to organism from oxidations, metabolic water, was considered as a constant of 250 ml. per diem in figures 1, 2, and 3. Insensible loss of water through skin and lungs as water vapor was also treated as a constant equal to 800 ml. per day in A. F. and M. H. who were small men and equal to 1000 ml. in R. H. a large man. Water loss in sweat was estimated; 1 liter was allowed when mean daily temperature was 80F and 2 liters were allowed when mean daily temperature was 85F.

Sodium and water exchanges of A. F. were distinctly more rapid than normal for 5 days. Thereafter exchange rates slowed down and cumulative deficit of water was materially reduced; this is not shown in graph.

Case summary 3 (M. H., No. 79429) and figures 3, 4, and 5 depict a phenomenal disturbance in renal physiologic regulation attending catheterization after an acute urinary obstruction had been superimposed upon a chronic obstruction at the neck of the bladder. For 2 days after the catheter was inserted, the rate of drinking and the rate of excretion of urine were within the ranges of those obtaining in diabetes insipidus. More remarkable were the large losses of sodium and water from the body. Within 43 hours almost all of the sodium of the extracellular compartment of a "normal" 60 kilogram (130 lb.) man* had been lost. Also lost, was four-fifths of the water that a normal man contains in his extracellular space, a volume of water that is roughly equal to 16 per cent of all the water in his body. These losses are all the more remarkable because the man had only a slight peripheral edema when the catheter was inserted. The recovery of the renal conservation of salt and water was slow; it began after 90 hours had elapsed when the excretion of salt and water began to fall behind the rate of intake of these substances. The recovery period is not graphed.

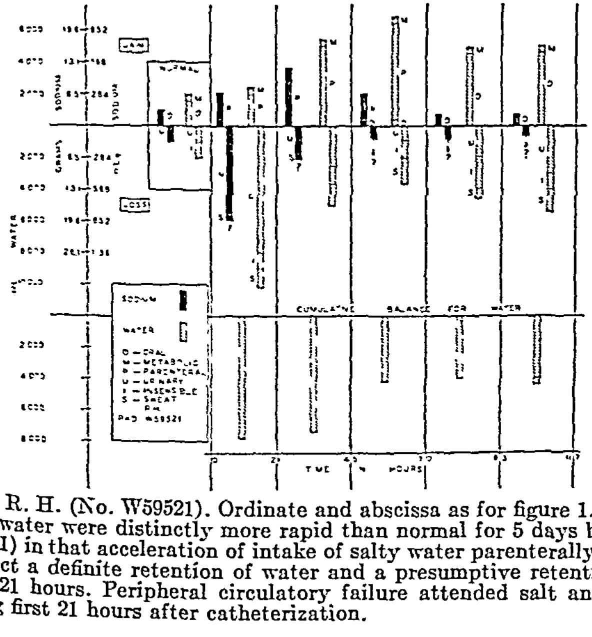

FIG. 2. Case R. H. (No. W59521). Ordinate and abscissa as for figure 1. Exchange rates of sodium and water were distinctly more rapid than normal for 5 days but R. H. differs from A. F. (fig. 1) in that acceleration of intake of salty water parenterally was sufficiently great as to effect a definite retention of water and a presumptive retention of salt after elapse of first 21 hours. Peripheral circulatory failure attended salt and water deficits incurred during first 21 hours after catheterization.

A. F. (No. 66068), a white man of 65 years, was admitted to Parkland Hospital at 4:00 p. m., January 26, 1949. He related a history of chronic urinary retention followed by acute complete retention for 3 days; self catheterization previously had been used frequently. Although he was dyspneic and had slight edema of his ankles, no other evidences of cardiac failure were found and he was permitted

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* The ECF compartment of the normal man averages 20 per cent of body weight and the sodium concentration in it is about 140 mEq. (3.22 G) per liter. Therefore the extracellular compartment of a normal man of 60 kg. weight would contain about 12 × 140 (3.22 G) or 1680 mEq. or 38.64 gm. of sodium. M. H. lost almost 1400 mEq. or 32 gm. of sodium within 43 hours.

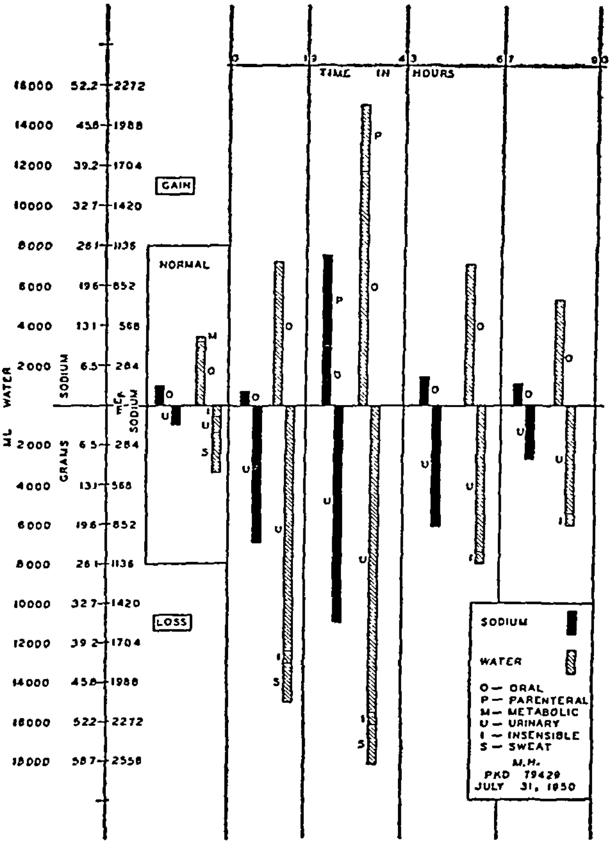

Fig. 3.

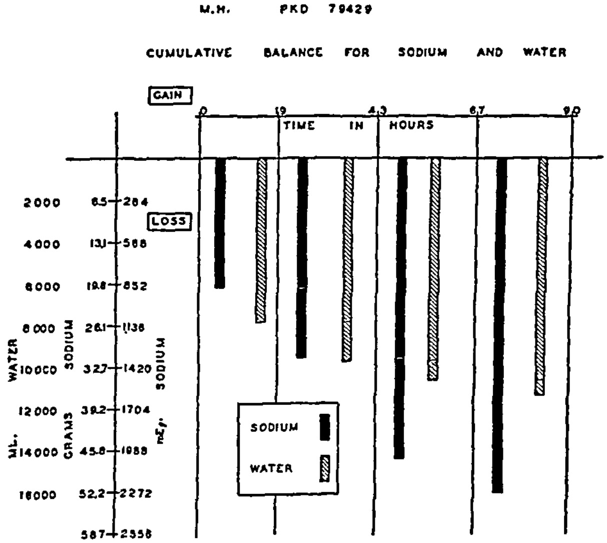

Fig. 4.

Figs. 3 and 4. Ordinates and abscissae are the same as in figure 1. Sodium and water inputs and sodium and water excretions were measured throughout period graphed. Metabolic gain of water and its insensible and sweat losses were estimated as in figure 1. Peripheral circulatory failure was imminent between nineteenth and forty-third hours only. Note in figure 4 that the water deficit was comparatively greater than sodium deficit during first 19 hours but sodium deficit was comparatively greater than water deficit thereafter. Plasma chloride concentration rose during first period and subsequently declined.

to walk to the ward. His blood pressure was 160/90 and the pulse rate was 126 per minute. The chloride concentration of plasma was found to be 597 mg. per cent (103 mEq/l), the carbon dioxide combining capacity to be 22 volumes per cent (10 mEq/l), and urea to be 310 mg. per cent. An indwelling catheter was inserted in the bladder and during the next 12 hours 8 liters of urine were passed. During the night, his respirations became deeper and more rapid despite the oral administration of 12 gm. sodium bicarbonate. Full doses of digitoxin were given. Later he had episodes of confusion and vomited a little. Fourteen hours after walking to the ward he became stuporous and, within another 2 hours, comatose. His blood pressure was then 100/56 and the pulse rate was 120 per

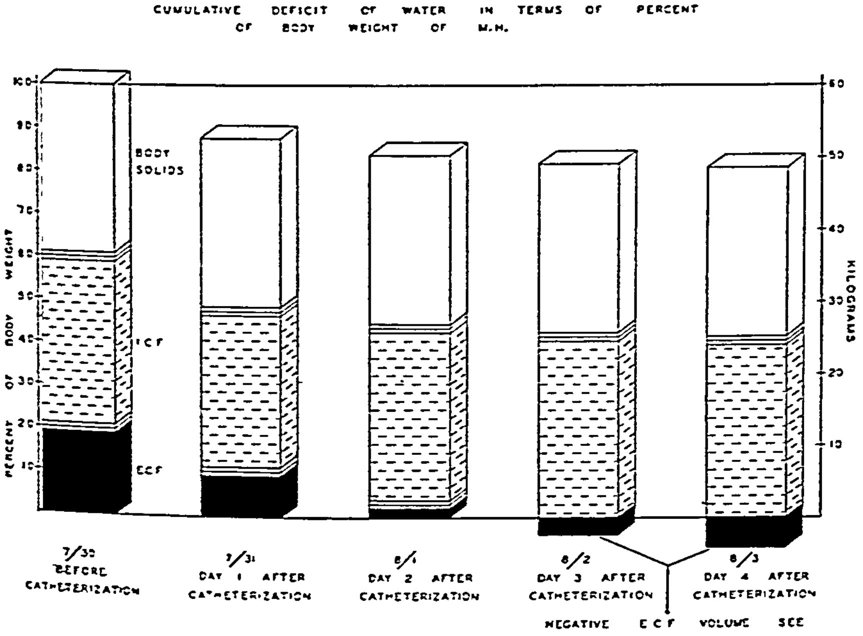

FIG. 5. Sodium and water contents of M. H. (60 kg.) were calculated assuming that 60 per cent of his initial body weight was water of which one-third, equal to 20 per cent of his body weight, was extracellular and remainder was intracellular; all of sodium was assumed to be extracellular as 140 mEq. (3.22G) per liter extracellular fluid. Therefore M. H. was calculated to have a total of 1,680 mEq. or 38.6 gm of sodium in his extracellular space before decompression of his bladder. Measured cumulative deficit of sodium was subtracted from above and remainder divided by 140; resultant (liters of extracellular fluid) was then transposed to per cent body weight and graphed.

It is clear that M. H. must have had a great deal more available sodium in his body than there was presumed to be in his extracellular space because his measured losses of sodium exceeded amount of this element that was calculated to exist about his cells. Bones and cells must have given up a large amount of sodium because M. H. did not die and he had only mild peripheral circulatory failure although the cumulative 4 day deficit of sodium amounted to 53 gm. sodium ion and that is equivalent to 132.56 gm. of sodium chloride the amount of salt contained in 14.73 liters of isotonic saline. If sodium and water had not been available from cells and bone, M. H. would have died with peripheral circulatory failure.

Above logic leads one to the question: how much sodium is deposited in bone and enters cells while chronic incomplete urinary obstruction exists? M. H.'s kidneys are now behaving normally in all respects, 7 weeks after this study was begun.

minute; respirations were of the Kussmaul type. The peripheral veins were empty; there were no peristaltic sounds and the abdomen was moderately distended. The deep tendon reflexes were absent and the muscles flaccid. The ankle edema was gone.

Because of the rapid development of the signs of severe salt depletion, and of acidosis, he was given intravenously one liter of M/6 sodium lactate solution to which was added 4 gm. of potassium chloride; a Levin tube was passed into his stomach and portions of a solution containing 16 gm. of sodium bicarbonate were given at frequent intervals through this tube. Within about 3 hours he had aroused from coma, was actually oriented but still sleepy. His blood pressure had risen to the precoma level of 160/88 and the pulse rate had decreased to 90 per minute. The plasma chloride concentration at that time was 574 mg. per cent (99 mEq/l); carbon dioxide combining capacity was 37 volumes per cent (17 mEq/l) and the urea concentration was 317 mg. per cent.

On the following day, January 28, 1949, he had again failed; he was sleepy, weak, nauseated, and his pulse rate had quickened to 110 per minute. The salt water deficit was greater than that which had been present at the conclusion of the sodium lactate therapy on the previous day. The further loss of salt was produced by the relatively rapid loss of 235 mEq. of sodium* salt in 3800 ml. of urine. The sodium deficiency had increased while the acidosis had diminished; the plasma carbon dioxide combining capacity was 44 volumes per cent (20 mEq/l). Consequently, one liter of M/6 sodium lactate and one liter of Ringer's lactate were given intravenously; an additional one liter of 10 per cent glucose in water was given to provide for the 24 hour insensible loss of water. One-half liter of blood was also administered. The next day, January 29, 1949, the patient had no nausea or vomiting and the respiration was of normal amplitude and rate. However, he felt weak, the pulse rate was 100 per minute, and the skin over his forehead was inelastic. The deficit in volume of salt water was still present because not enough salt had been given to replace the salt lost in the urine. Again, two liters of salt solution and one liter of glucose in water were given intravenously, and again the urinary and insensible losses exceeded the administered volume. So, on the next day (January 30, 1949) 4000 ml. of fluid (mainly Hartmann's solution) containing 426 mEq. of sodium (equivalent to 25 gm. of sodium chloride) were given. Following this therapy, his pulse rate was 70 per minute and he felt stronger even though the amount of urine excreted again exceeded the volume of fluids given. The plasma chloride concentration was 585 mg. per cent (101 mEq/l), the carbon dioxide combining capacity was 63 volumes per cent (29 mEq/l), the urea was 280 mg. He improved rapidly thereafter and was soon ambulatory and eating heartily.

R. H., a massive white man of 74 years, was admitted to Parkland Hospital at 4:00 p. m. on June 18, 1949. He was comatose and febrile. His skin was inelastic and his muscles were soft. His pulse varied between 120 and 140. A catheter was passed and 2700 ml. of urine were withdrawn. Subsequently the chemical examination of his blood showed a blood urea of 285 mg. per cent, a plasma chloride of 626 mg. per cent (107 mEq/l) and a carbon dioxide combining capacity of 28.8 volumes per cent (HCO_3 - 13 mEq/l).

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* An amount equivalent to 14 gm. sodium chloride.

Because of the presence of the physical signs of a sodium salt deficiency and the discovery of a low serum bicarbonate, one liter of Ringer's lactate and one liter of M/6 sodium lactate solution were given intravenously.

In spite of the administration of the saline solutions there was no visible improvement, in fact the signs of sodium need increased (his skin was more inelastic, his muscles were softer than the day before). So 4 liters of Ringer's lactate and 1 liter of 5 per cent glucose in water with 4 gm. of KCl in it were given intravenously and stupor superseded the coma. The blood urea had fallen to 47 mg. per cent, the plasma chloride concentration and the carbon dioxide combining capacity rose to 638 mg. per cent (110 mEq/l) and 71 volumes per cent (HCO_3-32 mEq/l) respectively. The physical signs of sodium salt deficit were still present although less evident and, in addition, the signs of pure water need appeared. Two liters of Ringer's lactate and 4 liters of glucose were given. The following day he was irrational and thirsty. He then drank 4300 ml. of water in which 7 gm. of salt were dissolved. The following day the signs of salt and water need were practically gone and he was rational, hungry, talked readily, and sat in a chair.

A Negro laborer, M. H. (No. 79429) 51 years old, was admitted to Parkland Hospital July 30, 1950 complaining of a peri-umbilical pain which had been present for 1 week. He had passed urine through perineal fistulas since 1928, and during the week before he entered the hospital, nocturia and frequency of urination had become worse. The blood pressure was 126/? and the mean temperature and pulse rate for that day were 98.6F and 74 per minute, respectively. He had slight pitting edema of the ankles. The next morning he was ambulatory and took breakfast and lunch. An indwelling catheter was inserted in his bladder at noon and 6 hours later 4500 ml. of urine had passed. The man's appearance had entirely changed; he was sleepy, movements of the arms and legs were made with great effort, and he remained in bed. His skin was inelastic, the ankle edema gone and his tongue wrinkled. The blood pressure was 110/70 and the pulse rate had increased to 98 per minute. His body weight was 126 pounds. The plasma chloride concentration was 580 mg. per cent (100 mEq/l) and the carbon dioxide combining capacity 42 volumes per cent (19 mEq/l); the blood urea was 171 mg. per cent. Milk was given for food because its sodium content is fairly constant and water was permitted ad libitum. By the end of 19 hours, the rate of volitional drinking of milk and water fell far behind the urinary flow rate so that 12,450 ml. of urine were passed but only 7200 ml. of milk and water were drunk. A net deficit of salt (as sodium chloride) of over 50 gm. was suffered during this exchange period by urinary loss even though the amount of salt ingested was 5 gm. which is an "average" salt intake for one day. All signs of sodium deficit which were present 12 hours previously were intensified; the blood pressure fell to 100/68. Within another 6 hours, the urinary flow had not abated and the man became weaker; the pulse was soft and the rate increased from 104 to 120 per minute when he was placed in a sitting position. The plasma concentrations were: chloride, 650 mg. (112 mEq/l); carbon dioxide combining capacity, 52 volumes per cent (23 mEq/l); urea, 105 mg.

The course of this illness indicated that the man might soon develop acute peripheral circulatory collapse unless intravenous salty fluids were given; consequently, 3500 ml. of Ringer's lactate were administered intravenously in two hours, and 1500 ml. of a saline-bicarbonate solution* were drunk. Improvement was definite; the blood pressure rose to 120/86, the pulse became full and the rate fell to 92 per minute. Thereafter a general diet was permitted. During this day the magnitude of the salt and water exchanges were phenomenol; over 15 liters of urine were passed† and about 16 liters of fluid were taken in by mouth and by vein. Expressing the amount of sodium found in the 15 liters of urine as sodium chloride, over 90 gm. salt were lost; this is approximately the total amount of sodium chloride expected to be present in the body of a man of his weight. Between the forty-third and sixty-seventh hours following catheterization, there was no alleviation of the signs of a moderate sodium deficit nor did they increase. The concentration of blood urea had fallen to 62 mg. per cent; the carbon dioxide combining capacity remained fairly constant at 55 volumes per cent (25 mEq/l), and the plasma chloride decreased to 580 mg. per cent (100 mEq/l). In the next 2 days, the volume of fluids ingested was approximately equal to the volume of urine, however an insufficient amount of salt was ingested. In the subsequent week, he continued to eat well and water and salt deficits were corrected as the urine volume diminished.

DISCUSSION

Normal renal function insofar as it pertains to the regulation of the body's content of sodium salts and water may be summarized as follows:

1) In the face of need of water by the body, the kidney excretes a small volume of urine with a high concentration of salts in it; 2) in the face of need of sodium salts the kidney excretes normal or subnormal volumes of urine having very little salt in it;‡ 3) when an excess of water exists in the body the kidney excretes a voluminous urine which contains little sodium; 4) and when an excess of salt exists in the body that salt is excreted with a great economy§ of water.[1]

These renal regulatory relationships are, in the normal man, so effective that the nonsweating man passing a normal volume of feces needs to take in less than a gram of sodium salts per diem to maintain his sodium store;[2, 3] within the range of physiologic adequacy;¶ he can drink water at a rate of 1 liter an hour and it will be excreted;[4] he may take in up to 35 gm. of sodium salts per day and they will be excreted without unduly increasing the mass of sodium in the body[4] and he can take in a little less than 2 liters of water each day in food and drink and yet is readily able to maintain the water content of his body.

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* A solution containing 3 gm. of sodium chloride and 1.5 gm. of sodium bicarbonate per liter of water.

† This volume of urine represents more water than that which is estimated to be present in all of M. H.'s extracellular and intravascular fluid.

‡ As low as 2 mEq of sodium salt per liter of urine.

§ 310 mEq of sodium salts per liter of urine.

¶ The restriction of the dietary salt to less than 1 gm. per diem is rarely attended by significant depletions of sodium stores even during the summer months in the Southwest provided that the individual does not engage in much physical labor.

[1] Peters, J. P.: Body Water. Springfield; Charles Thomas, 1935, chapter 11.

[2] Peters, J. P. and Van Slyke, D. D.: Quantitative Clinical Chemistry, Baltimore: Williams and Wilkins, 1932, vol. 1, p. 766.

[3] Ambard, Leo: Physiologie normal et pathoglogique des reins. Paris: Mason, 1920, 2nd ed.

During the development of urinary tract obstruction the body retains some water, salts,* and urea, and the base bicarbonate (carbon dioxide combining power) of the plasma is reduced.[5, 6] Therefore, the excretion of water and salts faster than they are taken in following the functional removal of the urinary obstruction can be considered physiologic as long as the excessive rates of excretion do not persist after the retentions of salt and water have been abolished. In other words, very high rates of excretion of water and salt after the removal of obstruction to the flow of urine are physiologically regulatory only so long as the body's stores of water and salt are above normal; should they persist until the body's stores of salts and water are severely depleted they must be looked upon as evidence of disturbed renal function and as physiologically vicious phenomena.

Unquestionably, the rapid rates of excretion of salt and water following decompression of the urinary tract are physiologic in a majority of cases, but it is equally unquestionable that in some instances they are not. Two of three cases presented here are examples of the extension of the excessive rates of the renal excretion of sodium salts and water far beyond the point where they could be considered physiologically compensatory reactions; every one of these men developed the indubitable signs of severe depletions of water and sodium salts before the renal excretion of these substances began to slow down.

One of them, R. H. (case 2), entered the hospital comatose with indubitable clinical signs of deficiencies of sodium salts and water yet he excreted 7800 ml. of water and 11 gm. of sodium more than he was given within 21 hours after the insertion of the catheter. The next day before salts and water were given, the signs of salt and water lack were much more pronounced than they were the day before. Surely, the reaction of this man's kidneys after catheterization was immediately inimical to his existence; for in spite of the obvious need for the conservation of salt and water that he showed when he was catheterized, his kidneys put out salt and water as if great excesses thereof existed.

Two of them, A. F. (case 1) and M. H. (case 3), were slightly edematous and they showed no signs of need for salt or water when the catheterizations were performed. However, within a matter of a few hours, A. F. suffered from peripheral circulatory failure brought on by the excretion of 5 liters more water than he took in. His excretion of salt during this period is unknown; it must have been great because the edema which was present when he was catheterized had disappeared and signs of salt need had appeared: empty veins, tachycardia, ileus, disappearance of tendon reflexes, flaccid muscles. Furthermore the administration of sodium salts and water parenterally and enterally quickly reversed the peripheral circulatory failure. M. H. (case 3) reacted similarly in that he showed signs of water and salt retention before decompression and thereafter quickly developed the signs of need for those substances. It is fairly clear that in all of these individuals the kidneys had temporarily lost their capacity for the conservation of salt and water during the time the urinary tract obstruction existed and that this capacity was not immediately regained.

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* Na, SO_4, HPO_4, organic acids.[6]

[4] Baird, M. M. and Haldane, J. B. S.: Salt and water elimination in man. J. Physiol., 56: 259, 1922.

[5] Keith, N. M. and Pulford, D. S. Jr.: Chloride retention in experimental hydronephrosis. J. Exper. Med., 37: 175, 1923.

[6] Peters, J. P., Wakeman, A. M., Eisenman, A. J. and Lee, C.: Total acidbase equilibrium of plasma in health and disease, X. The acidosis of nephritis. J. Clin. Invest., 6: 517, 1929.

M. H. has no significant hydronephrosis; the organic status of the kidneys of A. F. and R. H. were not determined with pyelography.

M. H. (case 3) is also interesting in other respects. His exchange of water (drinking and excreting) during the nineteenth to forty-third hours after decompression was within the range of that associated with diabetes insipidus, this immediately raises the question: what are the effects, if any, of a prolonged incomplete external urinary tract obstruction upon the activity of the pituitary gland?

M. H. also lost more sodium in his urine in 4 days than the amount calculated to be present in his extracellular compartment when he entered the hospital—(see fig. 5)—*but he did not die and he did not suffer* from peripheral circulatory failure. Doubtless, sodium and water must have come out of cells and bone in order to enable him to withstand their enormous losses through his kidneys. This observation raises the question: what are the effects of a urinary tract obstruction upon the sodium contents of cells and bone?

The practical aspects of these admittedly incomplete studies need some comment. Because serious salt and water depletions may follow decompression of the urinary tract they should be regularly expected. How may one determine their presence? The plasma chloride level is practically worthless as a sign; A. F.'s plasma contained 597 mg. per cent chloride as sodium chloride, R. H.'s contained 626 mg. per cent, and M. H.'s contained 580 mg. per cent while they were suffering from dangerous deficiencies of sodium salts and water. The plasma protein and hemoglobin concentrations are also relatively worthless because anemia and hypoproteinemia frequently attend chronic urinary tract obstructions. The concentration of chloride in the urine—Fantus test—is also worthless. High concentrations of salt, 2.5 to 4.0 gm. of NaCl per liter, were present in the urine of all these men while unquestionable salt and water deficiencies existed in them. The determination of the presence or absence of salt and water deficits rests upon the assessment of physical signs. Sodium salt water deficiency is manifested by: a loss of skin turgor, shrinking of the tongue, a softening of muscles, reduced filling of peripheral veins, slow filling of veins below a venous occlusive tourniquet, orthostatic hypotension early and recumbent hypotension later, softening of the pulse, tachycardia, depression of the central nervous system (apathy, aposia, sleepiness), anorexia, nausea, and shock—when the deficits become sufficiently great.

Additional signs appear when water is lost faster than salt. When this occurs, fever, disorientation, and dry mucous membranes are also often manifest. When salt is lost faster than water, tearing, salivation, diarrhea, headache, and muscle twitching may be seen in addition to the signs listed in the preceding paragraph.

Within recent years cognizance has been taken of the acidosis attendant upon urinary obstruction and alkaline sodium salts have been given with enormous benefit. Water and sodium are also provided thereby. However, if one administers only alkaline salts of sodium, the base bicarbonate deficit may be corrected long before sufficient water and sodium have been given. A. F.'s carbon dioxide combining power rose from 22 volumes per cent to 44 volumes per cent while the signs of salt water deficit increased. R. H.'s carbon dioxide combining capacity increased from 28.8 volumes per cent to 71 volumes per cent without the abolition of the signs of need of salt and water. M. H.'s carbon dioxide combining capacity rose from 42 volumes per cent to 52 volumes per cent while the salt and water deficits were increasing. It is clear that the correction of the acidosis with sodium lactate does not insure replenishment of the depleted extracellular volume.

A fair rule to follow may be stated as follows: When, after the correction of the acidosis, signs of salt and water deficits remain, Hartmann's solution (Ringer's lactate) should be given until the individual is out of danger from salt depletion. These studies of the changes in renal function occasionally attendant upon urinary decompression are very limited and incomplete. It is hoped that urologists will undertake to extend these studies: should balance-studies be undertaken that include the ascertainment of the renal exchange rates of sodium, potassium, calcium, magnesium, sulfate, phosphate, and organic acids during and following the relief of urinary obstruction much will be added to our knowledge of the patho-physiology of the kidney.

SUMMARY

The acute relief of a chronic lower urinary tract obstruction is occasionally attended by serious renal functional abnormalities characterized by so copious an excretion of sodium salts and water as to endanger life from salt and water depletion.

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ACUTE INTERMITTENT PORPHYRIA

WILLIAM M. IVERS

Cases of porphyria are usually presented to a group of internists rather than to a group of urologists. However, since this little known disease has become in the past 10 years recognized with increasing frequency more urologists will be asked to assist in the diagnosis.

By definition porphyria may be defined as a constitutional fault or inborn error in porphyrin metabolism. The porphyrins are red pigments found in such substances as hemoglobin, catalase, and myoglobin. They are closely concerned with cellular respiration. The basic structure of the porphyrins are four pyrrole rings connected by methane bridges and eight hydrogen atoms.

CLINICAL DESCRIPTION

Clinically, two reasonably distinct forms of the disease have been described: 1) the congenital or light sensitive form; 2) the intermittent acute form.

The acute form of the disease has a tendency to be familial. It is known that sulfonal, trional, or veronal will induce porphyria in certain individuals, and chiefly in women.

DIFFERENTIAL DIAGNOSIS

The variations in symptomatology and physical findings in the intermittent or acute type have without a doubt led to confusion in the diagnosis. For the most part these varying symptoms are either nervous or abdominal; yet, may be a combination of both. The nervous manifestations may be referable to any part of the nervous system (central, peripheral or autonomic). Porphyria should be considered in any obscure nervous disorder, especially unexplained peripheral neuritis, flaccid paralysis of extremities, bulbar palsy and hysteria. In obscure abdominal pain, examination for porphyria should be done. This disorder has been confused with gallstone colic, renal colic, appendicitis and lead poisoning. In gallstone colic the urine, Ehrlich reaction, may be positive due to excessive urobilinogen. The dark color of the urine plus the pain has confused porphyria with renal colic. Careful examination of the urine will obviate this error. The abdominal pain may be generalized or localized to any part of the abdomen or groins. The pain is severe and often difficult to control. The absence of muscle spasm and rebound tenderness distinguishes porphyria from appendicitis. Marked constipation is the rule.

POSITIVE DIAGNOSIS

The diagnosis is confirmed by finding uroporphyrin in the urine. Porphobilinogen is the colorless precursor of the principal pigments in porphyric urine. It apparently does not occur in the urine of the light sensitive type, but in this type large amounts of uroporphyrin appears and results in a red urine; whereas, in the intermittent type the urine is darker and more brown in color.

In the case presented the urine dripping from the ureteral catheter was color-

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less, but did color on exposure to light. During an acute episode porphobilinogen is usually present in large amounts and can be detected by using the Watson-Schwartz procedure, which is as follows:

1) Equal parts of urine and Ehrlich's reagent (2 ml. of each) are mixed in a test tube.

2) To the foregoing mixture is added an equal volume of a saturated aqueous solution of sodium acetate.

3 Two milliliters of chloroform are added to the whole and mixed thoroughly by vigorous shaking.

4) A positive result is indicated by persistence of a pink-purple color in the aqueous fraction after centrifugation. (In doubtful reactions re-extraction of the aqueous fraction with chloroform is helpful.)

It is a simple and a positive test. It is pathognomic of the disease. False positives are rare. At times it becomes necessary to determine the presence of urophyrin since porphobilinogen occurs irregularly in the so-called mixed porphyria and not at all in the light sensitive. This is done by spectroscopic examination.

CASE REPORT

The case reported is that of a 29 year old white man, who first consulted his family physician during September 1949, complaining of a general weakness and frequent sore throats. The physician felt that the chronic tonsillitis which the patient had had for sometime was the cause of his present malaise. His blood picture and urinalysis were normal and a tonsillectomy was performed on October 5, 1949. Postoperative recovery was uneventful.

One month following the tonsillectomy, the patient again presented himself complaining of nausea, vomiting, and acute abdominal pain localized in the region of the gallbladder and referred to the right shoulder. Eating of greasy or fatty foods aggravated the intestinal upsets. Subsequent x-rays revealed a nonfunctioning gallbladder. A cholecystectomy was done. The pathological diagnosis was chronic cholecystitis.

On the fourth postoperative day the patient apparently developed hematuria which subsided quickly without any cystoscopic diagnosis. He had an uneventful recovery and left the hospital in good condition. Examination following dismissal from the hospital revealed a slight anemia which responded to liver extract. During the month of December 1949, the patient was apparently in good condition.

On or about January 1, 1950, after a prolonged trip, the patient again developed nausea, vomiting, acute abdominal pain and weakness, particularly in the right arm. His wife stated his urine was often brown in color. He was again admitted, January 13, 1950, to the hospital for complete studies of an abdominal pain that was so severe it required large amounts of sedatives to control. The weakness or paralysis by the time of admission to the hospital had progressed throughout the entire body. The paralysis suggested poliomyelitis, but the spinal fluid was negative.

Urological consultation was requested because of the peculiar looking urine.

On cystoscopy the instrument was introduced without anesthesia and without pain. Several blood clots were evacuated from the bladder. Numerous petechiae were observed throughout the bladder mucosa. Catheters were introduced to each kidney and the urine from each was clear. Pyelograms were found to be normal. However, before the kidney urine specimens could be taken to the laboratory they had turned from crystal clear to a brownish color and for the first time a clue as to the disease with which we were dealing revealed itself. The segregated specimens showed no red blood cells per high power field. The urine was positive for porphobilinogen. Urine specimens were sent to the University of Colorado Medical School for spectroscopic studies.

Blood examination showed 6,550,000 red blood cells and 21,000 white blood cells with an essentially normal differential count. The bone marrow showed a normal hematopoietic tissue.

The paralysis progressed rapidly with loss of sphincter control. Calcium gluconate seemed to relieve the pain more than any other medication. Phenobarbital was not used after the diagnosis was made, because it is supposed to accentuate the condition. The patient expired on the fourth day following admission.

The positive pathological findings were acute porphyrinuria, demylination of the posterior roots of the spinal cord, and early degeneration of the anterior horn cells of the spinal cord.

The anatomic findings are consistent with intoxication with porphyrins. This is an acute condition and the clinical progress of the case coincides with that usually seen in acute porphyrinuria. This diagnosis is verified by finding the extremely high quantities of porphyrins in the postmortem urine.

COMMENTS

The finding of blood clots in the bladder at the time of cystoscopy caused considerable comment and speculation among the urologists. We concluded that due to the paralysis, the bladder became overdistended, this causing it to bleed.

In checking back over the family history it was revealed that several members of the immediate family had suffered similar conditions which have not been diagnosed and that the male members of the family have died in the late twenties or thirties of undiagnosed diseases.

This patient's abdominal distress during his spasms of pain was so intense and so uncontrolled by all forms of medication that my advice is, if you should see a similar case in such distress, curare might be the drug of choice.

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REFERENCES

Calvy, G. L.: Porphyria, a consideration in surgical diagnosis. Surg., Gynec. & Obst., 90: 716-721, 1950.

Hill, R. C., professor of biochemistry, University of Colorado (personal communication).

Howard, T. L.: Personal communication.

Watson, C. J.: A Textbook of Medicine, edited by R. L. Cecil, 7th edition. Philadelphia: W. B. Saunders Co., 1950.

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